Über dieses Buch

Dies ist ein digitales Exemplar eines Buches, das seit Generationen in den Regalen der Bibliotheken aufbewahrt wurde, bevor es von Google im Rahmen eines Projekts, mit dem die Bücher dieser Welt online verfügbar gemacht werden sollen, sorgfältig gescannt wurde.

Das Buch hat das Urheberrecht überdauert und kann nun öffentlich zugänglich gemacht werden. Ein öffentlich zugängliches Buch ist ein Buch, das niemals Urheberrechten unterlag oder bei dem die Schutzfrist des Urheberrechts abgelaufen ist. Ob ein Buch öffentlich zugänglich ist, kann von Land zu Land unterschiedlich sein. Öffentlich zugängliche Bücher sind unser Tor zur Vergangenheit und stellen ein geschichtliches, kulturelles und wissenschaftliches Vermögen dar, das häufig nur schwierig zu entdecken ist.

Gebrauchsspuren, Anmerkungen und andere Randbemerkungen, die im Originalband enthalten sind, finden sich auch in dieser Datei – eine Erinnerung an die lange Reise, die das Buch vom Verleger zu einer Bibliothek und weiter zu Ihnen hinter sich gebracht hat.

Nutzungsrichtlinien

Google ist stolz, mit Bibliotheken in partnerschaftlicher Zusammenarbeit öffentlich zugängliches Material zu digitalisieren und einer breiten Masse zugänglich zu machen. Öffentlich zugängliche Bücher gehören der Öffentlichkeit, und wir sind nur ihre Hüter. Nichtsdestotrotz ist diese Arbeit kostspielig. Um diese Ressource weiterhin zur Verfügung stellen zu können, haben wir Schritte unternommen, um den Missbrauch durch kommerzielle Parteien zu verhindern. Dazu gehören technische Einschränkungen für automatisierte Abfragen.

Wir bitten Sie um Einhaltung folgender Richtlinien:

+ *Nutzung der Dateien zu nichtkommerziellen Zwecken* Wir haben Google Buchsuche für Endanwender konzipiert und möchten, dass Sie diese Dateien nur für persönliche, nichtkommerzielle Zwecke verwenden.

+ *Keine automatisierten Abfragen* Senden Sie keine automatisierten Abfragen irgendwelcher Art an das Google-System. Wenn Sie Recherchen über maschinelle Übersetzung, optische Zeichenerkennung oder andere Bereiche durchführen, in denen der Zugang zu Text in großen Mengen nützlich ist, wenden Sie sich bitte an uns. Wir fördern die Nutzung des öffentlich zugänglichen Materials für diese Zwecke und können Ihnen unter Umständen helfen.

+ *Beibehaltung von Google-Markenelementen* Das "Wasserzeichen" von Google, das Sie in jeder Datei finden, ist wichtig zur Information über dieses Projekt und hilft den Anwendern weiteres Material über Google Buchsuche zu finden. Bitte entfernen Sie das Wasserzeichen nicht.

+ *Bewegen Sie sich innerhalb der Legalität* Unabhängig von Ihrem Verwendungszweck müssen Sie sich Ihrer Verantwortung bewusst sein, sicherzustellen, dass Ihre Nutzung legal ist. Gehen Sie nicht davon aus, dass ein Buch, das nach unserem Dafürhalten für Nutzer in den USA öffentlich zugänglich ist, auch für Nutzer in anderen Ländern öffentlich zugänglich ist. Ob ein Buch noch dem Urheberrecht unterliegt, ist von Land zu Land verschieden. Wir können keine Beratung leisten, ob eine bestimmte Nutzung eines bestimmten Buches gesetzlich zulässig ist. Gehen Sie nicht davon aus, dass das Erscheinen eines Buchs in Google Buchsuche bedeutet, dass es in jeder Form und überall auf der Welt verwendet werden kann. Eine Urheberrechtsverletzung kann schwerwiegende Folgen haben.

Über Google Buchsuche

Das Ziel von Google besteht darin, die weltweiten Informationen zu organisieren und allgemein nutzbar und zugänglich zu machen. Google Buchsuche hilft Lesern dabei, die Bücher dieser Welt zu entdecken, und unterstützt Autoren und Verleger dabei, neue Zielgruppen zu erreichen. Den gesamten Buchtext können Sie im Internet unter `http://books.google.com` durchsuchen.

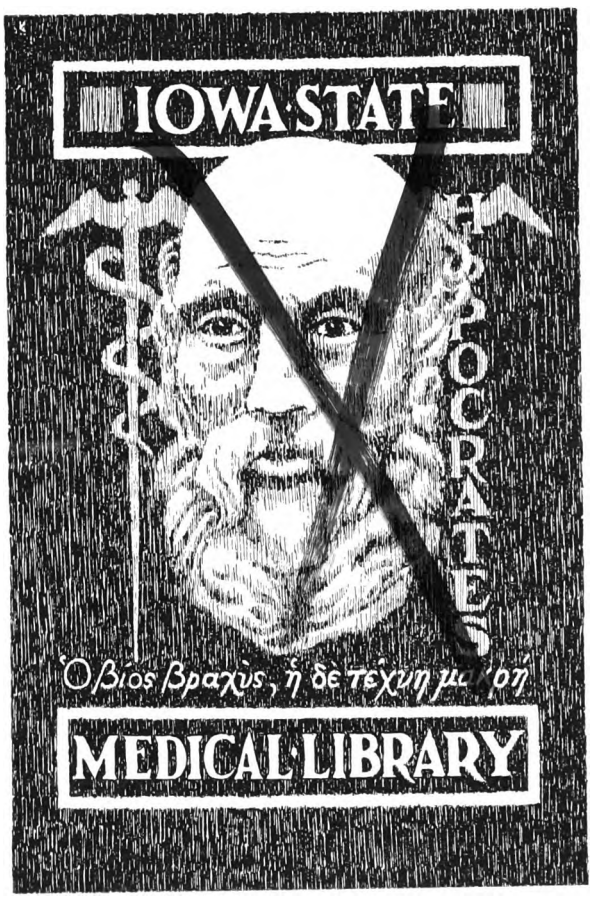
This is a reproduction of a library book that was digitized by Google as part of an ongoing effort to preserve the information in books and make it universally accessible.

Google™ books

https://books.google.com

HEALTH SCIENCE

UNIVERSITY OF IOWA
LIBRARIES



Digitized by Google

UNIVERSITY OF IOWA
3 1858 019 780 786

DATE DUE

DEMCO 38-297

Digitized by Google

Digitized by Google

Digitized by Google

Digitized by Google

WITHDRAWN

MARCH 5, 1949

MAR 31 1949

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

PAGES 381 TO 424

THE LANCET

Offices: 7, ADAM STREET, ADELPHI, W.C.2

Telegrams: LANCET, RAND, LONDON Telephone: TEMPLE BAR 7228 and 7229

No. X OF VOL. I, 1949
No. 6549 VOL. CCLVI

LONDON, SATURDAY, MARCH 5, 1949
Founded 1823 PUBLISHED WEEKLY Registered as a Newspaper

Pp. 88.—Price 1s.
Annual Subscription: £2 2s.

Digitized by Google

PLATO FOLDER

RE-ORDER NO. 2-102½LK

47185

Digitized by Google

MARCH 5, 1949 PAGES 381 TO 424

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6549 LONDON: SATURDAY, MARCH 5, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Retropubic Prostatectomy — TERENCE MILLIN, F.R.C.S. C. L. O. MACALISTER, F.R.C.S.E. P. M. KELLY, F.R.C.S. 381

Growth of the Preschool Child in London — A. T. GORE, D.P.A. W. T. PALMER 385

Paroxysmal Cold Hæmoglobinuria of Non-syphilitic Type — L. K. MALLEY, M.D. M. D. HICKEY, F.R.C.P.I. 387

Survival of Transfused Erythrocytes from a Donor with Nocturnal Hæmoglobinuria — J. V. DACIE, M.R.C.P. P. L. MOLLISON, M.R.C.P. 390

Œsophageal Lesions in Sclerodactyly — W. A. BOURNE, F.R.C.P. 392

Acquired Resistance to Proguanil (Paludrine) in *Plasmodium vivax* — D. R. SEATON, M.R.C.P. E. M. LOURIE, M.R.C.P. 394

Streptomycin in Non-gonococcal Urethritis — R. R. WILLCOX, M.B. 395

SPECIAL ARTICLES

Somatotypes and Medicine — J. M. TANNER, M.D. 405

Academic Salaries 407

THE WIDER WORLD

Nutrition and Health of Children in Five Countries of South America: 4. Peru — R. PASSMORE, D.M. 408

NEW INVENTIONS

Perspex Splint for Ulnar-deviation of the Fingers — C. B. HEALD, M.D. BRANDON LUSH, M.B. J. F. BUCHAN, M.B. 396

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents ... 409

LEADING ARTICLES

DEATH AMONG THE NEWBORN ... 399

HODGKIN'S DISEASE 400

BACTERIAL WARFARE 401

ANNOTATIONS

The Askwith Agreement Ends ... 402

Radiology of Congenital Intestinal Obstruction 403

Vitamin A and Bone Growth 403

Somatotypes 403

Chewing the Cud 404

The International B.C.G. Campaign 404

A Question of Cost 404

No Room at the Hospital 404

LETTERS TO THE EDITOR

Academic Freedom and the Health Act (Mr. R. T. Payne, F.R.C.S.) 411

Trichlorethylene as an Analgesic in Labour (Dr. P. W. Hopper) 411

Pyloric Hypertrophy with Eosinophil Infiltration (Mr. G. E. Moloney, F.R.C.S.E.) 412

Dietary Fat (Mr. A. R. P. Walker, PH.D.) 412

Veganin (Prof. Stanley Alstead, F.R.C.P.) 413

Tuberculous Lymph-node Perforation into Bronchi (Prof. Ph. Schwartz) 413

A Regeneration Substance? (Dr. A. P. N. Wedel; Prof. R. J. V. Pulvertaft, F.R.C.P.) 413

Palliative Surgery in Facial Palsy (Miss Josephine Collier, F.R.C.S.) 414

Prophylaxis of Ophthalmia Neonatorum (Dr. J. Jacobs) .. 414

A Picture Sought (Sir Adolphe Abrahams, F.R.C.P.) 415

Uræmia following Anæsthesia (Dr. F. B. Mallinson) 415

A Faculty of General Practice (Mr. T. B. Layton, F.R.C.S.) ... 415

Intestinal Diphtheria (Major-General Djamil Faïk Tutunji). 416

Health Centres Now? 416

Streptomycin in Whooping-cough (Dr. D. P. Nicholson) 416

Clinical Estimation of Basal Metabolic Rate (Dr. Eugene Bene) 416

Management of Peptic Ulcer (Dr. D. H. Belfrage) 417

Mesenteric Adenitis (Mr. V. A. J. Swain, F.R.C.S.) 417

Myasthenia Gravis 417

Hospital Biochemists (Mr. D. Watson) 417

REVIEWS OF BOOKS

Hæmolysis and Related Phenomena 397

Juvenile Rheumatism 397

The Practice of Group Therapy. 397

Streptomycin und Tuberkulose. 397

A-B-C's of Sulfonamide and Antibiotic Therapy 397

Glomerular Nephritis 398

Physiology of the Eye 398

Psychology of Personality 398

Experimental Diabetes Mellitus .. 398

Youth in Despair 398

PUBLIC HEALTH

Tuberculosis in London 418

Influenza 418

Scotland's Vital Statistics for 1948 418

PARLIAMENT

Safe Milk 418

Adoption of Children 419

Question Time 419

OBITUARY

Sir William Hale-White 421

NOTES AND NEWS

Training Grants for Assistants ... 422

Courses in Natural Science 422

Detection by Telepathy 422

Indian Drug Research Institute .. 422

Reorientations in Neurology 422

The Assistance Publique 422

New Journal on Nursery Schools 423

Memories of a Surgeon 423

Swedish Puzzle 423

University of Liverpool 423

Leeds Postgraduate Course 423

Diary of the Week 424

Appointments 424

Births, Marriages, and Deaths ... 421

—E. & S. LIVINGSTONE, LTD., *Medical Publishers*, Teviot Place, Edinburgh—

★ A Selection of Outstanding New Books ★

PATHOLOGY OF THE NERVOUS SYSTEM

Second Edition. By J. HENRY BIGGART, C.B.E., M.D., D.Sc. With foreword by A. MURRAY DRENNAN, M.D., F.R.C.P.E., F.R.S.E. 344 pages. 232 Illustrations. 21s.

TEXTBOOK OF MEDICAL TREATMENT

Fifth Edition. By Professor D. M. DUNLOP, B.A., M.D., F.R.C.P., Professor L. S. P. DAVIDSON, B.A., M.D., F.R.C.P., and Professor J. W. McNEE, D.S.O., M.D., F.R.C.P. With 35 Eminent Contributors. 1016 page. Illustrated. 35s

HANDBOOK OF SURGERY

Second Edition. By ERIC C. MEKIE, M.B., Ch.B., F.R.C.S. (Edin.), and IAN MACKENZIE, M.B.E., M.B., Ch.B., F.R.C.S. (Edin.). 780 pages. Illustrated. 20s.

CRITICAL STUDIES IN NEUROLOGY

By F. M. R. WALSHE, M.D., F.R.S. 272 pages. 16 Illustrations. 15s.

TEXTBOOK OF MEDICINE

Ninth Edition. By Sir JOHN CONYBEARE, K.B.E., M.C., D.M. (Oxon.), F.R.C.P. Assisted by 18 Eminent Contributors. 892 pages. Illustrated. 30s.

INTRODUCTORY BOTANY

By ALEXANDER NELSON, B.Sc. (Glas.), Ph.D., D.Sc. (Edin.). 488 pages. 121 Illustrations. 22s. 6d.

MEDICINE

By A. E. CLARK-KENNEDY, M.D., F.R.C.P. In two volumes, sold separately. Vol. I: The Patient and his Disease. 20s. Vol. II: Diagnosis, Prevention and Treatment. 25s.

As from the March issue (Vol. XXI, Part I) the **BRITISH JOURNAL OF UROLOGY**, under the Editorship of Mr. David Band, F.R.C.S. (Edin.), will be published by E. & S. LIVINGSTONE, LTD. Subscription price £2 2s. per annum (4 issues).

Digitized by Google

OXFORD MEDICAL PUBLICATIONS

KAYNE, PAGEL, AND O'SHAUGHNESSY'S PULMONARY TUBERCULOSIS

Pathology, Diagnosis, Management and Prevention

Revised and partly rewritten by

WALTER PAGEL, *M.D.*
Pathologist, Central Middlesex County Hospital

F. A. H. SIMMONDS, *M.D., D.P.H.*
Medical Director, Clare Hall County Hospital, Middlesex

N. MACDONALD, *M.B., M.R.C.P.*
Physician to the Chest Clinic, Redhill County Hospital, Middlesex

L. FATTI, *F.R.C.S.*
Thoracic Surgeon, Hillingdon County Hospital and Harefield County Hospital, Middlesex

SECOND EDITION 738 pages 288 illustrations 63s. net

SOME COMMON PSYCHOSOMATIC MANIFESTATIONS

by J. BARRIE MURRAY, *M.D., M.R.C.P.*
Diagnostic Physician, Tavistock Clinic; Physician to Bolingbroke Hospital and the Margaret Street Hospital for Diseases of the Chest, London

114 pages 7s. 6d. net

PSYCHOTHERAPY: ITS USES AND LIMITATIONS

by D. R. ALLISON, *M.D., M.R.C.P.*
Physician to Stockport Infirmary
and
R. G. GORDON, *M.D., D.Sc., F.R.C.P.*
Consulting Neurologist to Stoke Park Colony

168 pages 8s. 6d. net

MANAGEMENT IN OBSTETRICS

by ANDREW M. CLAYE, *M.D., F.R.C.S., F.R.C.O.G.*
Professor of Gynæcology and Obstetrics in the University of Leeds

196 pages 17 illustrations 12s. 6d. net

THE BACKGROUND OF THERAPEUTICS

by J. HAROLD BURN, *M.D., F.R.S.*
Professor of Pharmacology in the University of Oxford

376 pages 59 illustrations 26 tables 22s. 6d. net

A PRACTICAL MANUAL OF DISEASES OF THE CHEST

by MAURICE DAVIDSON, *M.D., F.R.C.P.*
Physician to the Brompton Hospital for Consumption and Diseases of the Chest: Associate Physician to the Royal Cancer Hospital

THIRD EDITION 686 pages 281 illustrations 50s. net

OXFORD UNIVERSITY PRESS

Digitized by Google

MARCH 12, 1949 PAGES 425 TO 464

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6550 LONDON: SATURDAY, MARCH 12, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Value of Systemic Penicillin in Finger-pulp Infections — S. H. HARRISON, F.R.C.S.; ELIZABETH TOPLEY, M.B.; J. LENNARD-JONES, B.A. 425

A Clinical Method of Assessing Analgesics — A. J. H. HEWER, M.B.; C. A. KEELE, F.R.C.P.; K. D. KEELE, M.R.C.P.; P. W. NATHAN, M.R.C.P. 431

March Hæmoglobinuria — M. LUBRAN, M.B.; J. SAKULA, M.R.C.P. 435

Inhalation of Stomach Contents — A. WILLCOX, F.R.C.P. 438

A Tuberculin-neutralising Factor in the Serum of Patients with Sarcoidosis — A. Q. WELLS, D.M.; J. A. H. WYLIE, M.D. 439

PRELIMINARY COMMUNICATION

Streptomycin-Streptokinase Treatment of Tuberculous Meningitis — I. A. B. CATHIE, M.D. 441

THE WIDER WORLD

Nutrition and Health of Children in Five Countries of South America: 5. Colombia — R. PASSMORE, D.M. 450

SPECIAL ARTICLES

Whither Medicine? 451

REVIEWS OF BOOKS

Practice of Endocrinology. Raymond Greene, M.R.C.P. 442

Coöperation, Tolerance and Prejudice. Samuel Lowy, M.D. 442

Heart. A. A. Luisada, M.D. 442

LEADING ARTICLES

THE CUTS 443

TREATMENT OF THE INFECTED HAND 443

INFECTED AIR 444

HÆMOGLOBINURIA 445

ANNOTATIONS

Towards a New Deal 446

New Hope for the Old 447

Health Centres 447

The Undescended Testicle 448

Sexual Offenders 449

Cancer of the Breast 449

Index to THE LANCET 449

DISABILITIES

25. Stammering 452

LETTERS TO THE EDITOR

Academic Freedom and the Health Act (Dr. W. Russell Brain) 454

Fellowship for Freedom in Medicine (Dr. W. A. Bourne) .. 454

Practice Outside the Service (Dr. Beryl Harding) 455

The Optician's Training (Mr. G. H. Giles) 455

National Formulary (Prof. A. E. Barnes, F.R.C.P., and others) ... 455

Miracil D (Dr. D. M. Blair) 456

A Picture Sought (Dr. D. N. Baron) 456

Splenectomy in Kala-azar (Dr. F. Murgatroyd) 456

Hospital Biochemists (Mr. R. A. Ward, F.I.M.L.T.) 456

Independence in Research (Mr. F. S. A. Doran, F.R.C.S.) 456

Female Circumcision in the Sudan (Sir Basil Neven-Spence, M.D., M.P.) 457

Chewing the Cud (Mr. John Roberts, F.R.C.S.) 457

Gastric Carcinoma (Dr. Denys Jennings) 457

No Room at the Hospital 458

A Faculty of General Practice (Dr. W. Edwards; Dr. Harold Leeson) 458

Gum-saline (Mr. Bryan Williams, F.R.C.O.G.) 458

Medical History of the War (Prof. F. A. E. Crew, F.R.C.P., F.R.S.) .. 458

Subscriptions to THE LANCET 459

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 453

PARLIAMENT

Analgesia in Childbirth 459

Question Time 460

PUBLIC HEALTH

Influenza 461

Expulsion of Vaccine Lymph 461

Notification of Infectious Diseases 461

Industry in 1947 461

NOTES AND NEWS

New Remedy for Seasickness 462

Care of the Old in their Homes .. 462

Review of Convalescent Homes .. 462

The Guy's Dental School 462

Adaptation of E.M.S. Huts 463

Film on the Prolapsed Disc 463

Exchange Holidays 463

University of Oxford 463

University of Cambridge 463

Royal College of Physicians of London 463

Royal College of Surgeons of England 463

Course on Rheumatism 463

World Health Organisation 463

Ophthalmic Practitioners' Fees .. 464

Society of Medical Officers of Health 464

Diary of the Week 464

Appointments 464

Births, Marriages, and Deaths ... 461

Antispasmodic and Sedative

NEURO-TRASENTIN

Regd. Trade Mark

Combines the sedative effect of phenobarbitone with the antispasmodic action of Trasentin on smooth muscle.

It may be used in all cases of

SPASM OF THE GASTRO-INTESTINAL AND GENITO-URINARY TRACTS

Apply for a sample and literature to

CIBA LABORATORIES LIMITED · HORSHAM · SUSSEX

Telephone: Horsham 1234 Telegrams: Cibalabs, Horsham

1/48

Digitized by Google

VITAMINS PLUS— WHAT?

There's more than vitamins in SevenSeaS

The vitamin story is not the whole story—the vehicle which carries them and the manner in which they are carried are of great significance. Vitamins A and D, as well as pro-vitamin A, are fully efficient only when they are dissolved in oil.

But what of the oil? And of the manner in which the vitamins are associated with it? Isolated or synthesized vitamins dissolved in oil are not the same thing as the natural combination of the vitamins with the oil that characterizes cod liver oil.

Cod liver oil is richer in metabolically important unsaturated and readily digestible fats than any other edible oil or fat. Unsaturated fats are important in themselves and are doubly so when, as in the case of cod liver oil, the vitamins are an integral part of them.

SevenSeaS cod liver oil, extracted at sea from fresh livers, presents both the unsaturated fats and the fat soluble vitamins in their ideal combination for meeting nutritional needs and especially those of convalescents, mothers, and children.

STANDARD OIL

Vitamin A - 20,000 I.U.
Vitamin D - 2,500 I.U. per oz.

CONCENTRATED OIL CAPSULES

Vitamin A - 60,000 I.U.
Vitamin D - 6,000 I.U. per oz.

SEVENSEAS
COD LIVER OIL

BRITISH COD LIVER OILS
(HULL & GRIMSBY) LIMITED
ST. ANDREW'S DOCK, HULL, ENGLAND

ABRIL CORPORATION (GT. BRITAIN) LTD.
PHARMACEUTICAL DIVISION · BRIDGEND · GLAM.

ANNOUNCING

Autosorb

READILY ABSORBABLE

SURGEON'S GLOVE POWDER

Specially formulated to obviate post-operative morbidity due to talc granuloma in surgical practice.

SAMPLES AND LITERATURE AVAILABLE ON REQUEST FROM THE MANUFACTURERS

supplementing the diet

At the present time, the necessity for a sound diet containing a good supply of vitamins cannot be over-emphasised. Although there is some diversity of opinion as to the usefulness of administering synthetic vitamin supplements, it is generally agreed that the inclusion in the diet of natural foods of high vitamin content is most desirable.

Marmite, which is a yeast extract, contains naturally-occurring essential vitamins of the B_2 complex. One of the chief advantages of using Marmite is that, while it provides a useful source of B_2 vitamins, it also adds a delicious flavour to soups, stews, savoury dishes and sandwich-spreads. An appetising drink can be made by mixing Marmite with hot water or milk.

MARMITE
yeast extract
contains
Riboflavin (vitamin B_2) 1.5 mg. per oz.
Niacin (nicotinic acid) 16.5 mg. per oz.
Jars: 1-oz. 8d., 2-oz. 1/1, 4-oz. 2/-, 8-oz. 3/3, 16-oz. 5/9
Obtainable from Chemists and Grocers
Special terms for packs for hospitals, welfare centres and schools
Literature on request
THE MARMITE FOOD EXTRACT CO. LTD.
35, Seething Lane, London, E.C.3
4811

Digitized by Google

MARCH 19, 1949 PAGES 465 TO 508

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6551 LONDON: SATURDAY, MARCH 19, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

The Syndrome of Diabetes Mellitus and its Causes — Prof. H. P. Himsworth, F.R.C.P. ... 465

Injuries and Death from Lightning — Major M. J. G. Lynch, M.R.C.P. Major P. H. Shorthouse, M.R.C.S. ... 473

Tuberculous Abscess at the Site of Penicillin Injections — G. B. Forbes, M.B. F. G. St. Clair Strange, F.R.C.S. ... 478

Long-acting Preparation of Testosterone — Prof. E. Carlinfanti, M.D. F. D'Aló L. Cutolo ... 479

A Wheel-chair — A. G. B. Poole, M.B. ... 480

MEDICAL SOCIETIES

Edinburgh Obstetrical Society: Incoördinate Uterine Action ... 482

SPECIAL ARTICLES

Hospital Medical and Dental Staff: Terms and Conditions of Service ... 491

Streptomycin in Britain ... 496

REVIEWS OF BOOKS

Critical Studies in Neurology. F. M. R. Walshe, F.R.C.P.; F.R.S. 483

Detailed Atlas of the Head and Neck. Prof. R. C. Truex, M.S., C. E. Kellner ... 483

Anæsthesia for the Poor Risk. W. W. Mushin, M.B. ... 483

Tuberculosis. Prof. F. M. Pottenger, F.A.C.P. ... 483

The Modern Management of Gastric and Duodenal Ulcer. F. C. Deller, M.D. ... 484

Review of Plastic and Reconstructive Surgery. Prof. E. C. Padgett, M.D., K. L. Stephenson, M.D. ... 484

LEADING ARTICLES

Specialists' Salaries ... 485

Names for Blood-cells ... 486

Malignant Hypertension ... 487

ANNOTATIONS

The King ... 488

Neurological Disorders in Periarteritis Nodosa ... 488

Where Should Medicine be Taught? ... 488

Anti-histamine Drugs in the Common Cold ... 489

Systolic Murmurs ... 489

How to Tell the World ... 490

Postgraduate Education in Australia ... 490

LETTERS TO THE EDITOR

Objects of Research (Dr. A. A. Osman) ... 498

Lymphocytes and Intravascular Hæmolysis (Mr. W. T. Catton, M.Sc.) ... 498

Sheffield Registrars' Group (Dr. R. S. Weetch) ... 499

Management of Peptic Ulcer (Dr. S. C. Lewsen) ... 499

Health Centres Now? (Dr. J. W. Nicholas) ... 499

Hodgkin's Disease (Dr. R. F. Hendtlass) ... 500

Practice Outside the Service (Dr. S. Graham) ... 500

Veganin (Mr. Eliot Warburton) ... 500

Peptic Disorders in a Family (Dr. C. H. Bateman) ... 500

The Cuts ... 500

Diabetes (Dr. J. L. Blair) ... 501

Posture for Liver Biopsy (Prof. Emery Schill, M.D.) ... 501

Hæmoglobinuria (Dr. J. V. Dacie) 501

Bacterial Warfare (Dr. J. V. Walker) ... 501

Inhalation of Stomach Contents (Dr. P. R. Bromage; Dr. Hoël Parry-Price) ... 501

A Picture Sought (Mr. R. H. Gardiner, F.R.C.S.) ... 502

Trichlorethylene in Labour (Dr. Wright Lambert; Dr. John Elam; Dr. Gilbert Burnet) ... 502

Retropubic Prostatectomy (Mr. T. L. Chapman, F.R.C.S.) ... 502

The Nicotinic-acid Tolerance Test (Dr. A. Erdei) ... 503

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents ... 497

PUBLIC HEALTH

Influenza ... 503

Yellow Fever in Panama ... 503

The Future of Mass Radiography 503

PARLIAMENT

Question Time: Fat-content of Ice-cream—Tuberculosis in the Navy—Patients' Travelling Expenses—Cremation Certificates—Remuneration for Temporary Residents ... 504

OBITUARY

George Cockcroft ... 504

Ethel Vaughan-Sawyer ... 505

NOTES AND NEWS

Appeal Tribunal ... 506

Cambridge Examinations ... 506

Indian Medical Research ... 506

Centenary at Watford ... 506

A G.P. Looks Back ... 506

University of Oxford ... 506

Ophthalmological Society of the United Kingdom ... 506

Royal College of Surgeons of England ... 507

Royal Microscopical Society ... 507

British Schools Exploring Society 507

Chair of Pædiatrics for Wales ... 507

Medical Society of London ... 507

World Health Organisation ... 508

Diary of the Week ... 505

Appointments ... 508

Births, Marriages, and Deaths ... 508

Second Edition Now available

SURGERY: A Textbook for Students

By CHARLES AUBREY PANNETT, B.Sc., M.D., F.R.C.S.

Professor of Surgery, University of London; Director of the Surgical Unit, St. Mary's Hospital, London; sometime member of the Court of Examiners R.C.S. Eng., and Examiner to the Universities of London, Manchester, and Cardiff

769 + xiv. **Price 27s. 6d. net, plus 1s. postage**

Extensively illustrated throughout text

HODDER & STOUGHTON LTD. 20, WARWICK SQUARE, LONDON, E.C.4

Digitized by Google

OXFORD MEDICAL

PUBLICATIONS

Some Recent Publications

KAYNE, PAGEL, and O'SHAUGHNESSY'S PULMONARY TUBERCULOSIS

Revised and partly rewritten by WALTER PAGEL, *M.D.*, F. A. H. SIMMONDS, *M.D.*, *D.P.H.*, N. MACDONALD, *M.B.*, *M.R.C.P.*, and L. FATTI, *F.R.C.S.*

SECOND EDITION 738 pages 288 illustrations 63s. net

SOME COMMON PSYCHOSOMATIC MANIFESTATIONS

by J. BARRIE MURRAY, *M.D.*, *M.R.C.P.*

114 pages 7s. 6d. net

POST MORTEM APPEARANCES

by JOAN M. ROSS, *M.D.*, *B.S.*, *M.R.C.S.*, *L.R.C.P.*

FIFTH EDITION 318 pages 8s. 6d. net

CUNNINGHAM'S MANUALS OF PRACTICAL ANATOMY

Volume I. General Introduction. Upper Limb. Lower Limb.

Revised and edited by J. C. BRASH, *M.C.*, *M.D.*, *F.R.C.S.*, *F.R.S.E.*

ELEVENTH EDITION 408 pages 200 illustrations (112 in colour) 21s. net

OXFORD UNIVERSITY PRESS

PROTECTING YOUNG TEETH

In recommending a dentifrice for children's use, three major factors will influence your selection.

(a) It is of obvious importance that the cleansing agents employed should be completely free of abrasive action.

(b) Powerful astringents are contra-indicated, as these may irritate and inflame the gum membrane.

(c) The essential oils incorporated must have a pleasant appeal to the young patient.

In all these respects, Phillips' Dental Magnesia presents a dentifrice which can, with confidence, be recommended to children of all ages. Completely free from harmful ingredients, it possesses a unique flavour which makes a very strong appeal to the young. Phillips' Dental Magnesia has, moreover, the outstanding property of inhibiting oral acidity by reason of the 'Milk of Magnesia'★ content, a very real advantage in protecting young teeth.

Phillips' Dental Magnesia (Regd.)

THE CHAS. H. PHILLIPS CHEMICAL CO., LTD. 1, WARPLE WAY, LONDON, W.3.

★ *'Milk of Magnesia' is the trade mark of Phillips' preparation of magnesia.*

Digitized by Google

MARCH 26, 1949 PAGES 509 TO 552

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6552 LONDON: SATURDAY, MARCH 26, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

At the Cross-roads: the Development of Our Health Services — A. L. BANKS, F.R.C.P. 509
The Action of Dihydroergocornine on the Circulation — Prof. R. H. GOETZ, M.D. 510
Immediate Results of Partial Gastrectomy for Peptic Ulcer — B. B. MILSTEIN, F.R.C.S. 514
Agranulocytosis and Thrombocytopenia Following the Use of Tridione — T. W. FORSTER, M.B., J. W. WATSON, M.B., E. NEUMARK, M.B. 517
Necrotic Jejunitis — K. A. FICK, M.D., Captain A. P. WOLKEN, M.D. 519
Effect of Intra-uterine Radium Therapy on Ovarian Function — GERTRUDE GOLDSCHEIDER, M.D. 521
Use of Thrombin in Liver Puncture — L. FRIEDRICH, M.D., M. POLICZER, M.D. 523

SPECIAL ARTICLES

The Reflecting Microscope — ROBERT BARER, M.B. 533
Propagation of Mouse Tumours by Means of Dried Tissue 535
On Knowing Men 535
New Zealand Hospital Salaries .. 537

NEW INVENTIONS

Modified Stand for Sedimentation Tubes — Prof. A. ST. G. HUGGETT, M.B. 524

REVIEWS OF BOOKS

Trace Elements in Food 525
Techniques in Physiotherapy 525
Occupational Therapy Source Book 525
Joseph Lister: the Friend of Man 525
Radio-active Indicators 525
Principles of Biological Assay ... 526
Pathologie des Kohlehydratstoffwechsels 526

LEADING ARTICLES

FURTHER THOUGHTS ON SPECIALIST SALARIES 527
RADIO-IODINE IN THYROTOXICOSIS 528
HEALTH INSURANCE IN AMERICA 529

ANNOTATIONS

Marrow Biopsy 530
Amyloidosis in Rheumatoid Arthritis 531
W.H.O. Plans for the Future 531
Coronary Thrombosis 532
F.R.S. 532
The King's Health 532

DISABILITIES

26. Enuresis 537

LETTERS TO THE EDITOR

The Undescended Testicle (Mr. Denis Browne, F.R.C.S.) 543
Health Centres Now? 543
Clinical Estimation of Basal Metabolic Rate (Dr. Raymond Greene) 543
Lymphocytes and Intravascular Hæmolysis (Dr. R. H. Trinick) 544
National Formulary (Dr. A. Forster) 544
Female Circumcision in the Sudan (Dr. A. O. Abu Shamma and others) 544
Practice Outside the Service 545
Medical Treatment Abroad (Dr. B. G. Edelston) 545
Liver Extracts (Mr. G. E. Shaw, B.SC.) 545
Benadryl in Parkinsonism (Dr. E. Montuschi) 546
Inhalation of Stomach Contents (Dr. Samuel Lask) 547
Veganin (Prof. Stanley Alstead, F.R.C.P.) 547
Nitrogen Mustard in Bone Tuberculosis (Prof. Julian Aleksandrowicz, M.D.) 547
Retropubic Prostatectomy (Mr. H. K. Vernon, F.R.C.S.) 547
Arab Refugees (Mr. Victor Gollancz) 547
Heroin (Dr. J. Hartsilver) 547
How to Tell the World (Dr. W. Hartston) 548
Intensive Treatment of Schistosomiasis with Sodium Antimonyltartrate (Dr. G. A. Rail) 548
Sterilisation of Polythene Tubing (Dr. John Murray) 548

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 542

PARLIAMENT

Analgesia in Childbirth 539
Artificial Insemination and the Law 540
Medical Treatment Abroad 540
R.A.F. Medical Service 541
Question Time 541

PUBLIC HEALTH

Infant Vaccination 549
Births and Marriages in 1946 549
Influenza 549
Whale-meat Regulations 549

OBITUARY

Karolina Widerström 550

NOTES AND NEWS

Senior Hospital Medical Officers .. 550
Progress in Mental Health 550
Parliamentary Footnote 551
Anxieties of Married People 551
Dostoïevsky's Illness 551
Electrotherapy 551
University of Cambridge 551
University of Manchester 551
University of Durham 552
University of Leeds 552
University of Aberdeen 552
Pædiatric Congress 552
Liverpool Hospital Regional Board 552
Health Centres 552
Diary of the Week 549
Appointments 552
Births, Marriages, and Deaths ... 550

Third Edition 12s. 6d. net, plus 8d. postage

INTRODUCTION TO
DISEASES OF THE CHEST

By JAMES MAXWELL, M.D. (Lond.), F.R.C.P. (Lond.)

Physician, Royal Chest Hospital; Physician to the Ministry's Mass X-ray Unit; Consulting Physician, Royal National Sanatorium, Bournemouth; late Physician, St. Bartholomew's Hospital

Demy 8vo 308 + xii 66 Half-tone Illustrations

HODDER & STOUGHTON LTD. 20, WARWICK SQUARE, LONDON, E.C.4

Digitized by Google

NEW TEXTBOOKS
for
STUDENTS and PRACTITIONERS
preparing for the Higher Examinations

HANDBOOK OF MEDICINE FOR FINAL YEAR STUDENTS
by G. F. WALKER, M.D., M.R.C.P., D.C.H.
This well-known book has been completely revised and brought up to date. Previous editions have met with an enthusiastic reception. Valuable for M.R.C.P. candidates. *4th Edition* *Pp.* 305 *Price*, 25*s. net.*

HANDBOOK OF MIDWIFERY
by MARGARET PUXON, M.D., M.R.C.O.G.
Specially useful for the higher examinations, D.R.C.O.G., M.R.C.O.G., etc. *Just published* *Pp.* 326 *Price*, 25*s. net.*

HANDBOOK OF VENEREAL INFECTIONS
by R. GRENVILLE-MATHERS, M.A., M.D. Cantab.
An exposition of modern treatment by Penicillin. Valuable for specialists in this field. *Pp.* 116 *Price*, 12*s.* 6*d. net.*

HANDBOOK OF OPHTHALMOLOGY
by J. H. AUSTIN, M.B., D.O.M.S., D.O. Oxford.
Intended for candidates preparing for the higher examinations, D.O.M.S. and D.O. Oxford. In preparation. *Price*, 30*s. net.*

HANDBOOK OF DENTAL SURGERY AND PATHOLOGY
by A. E. PERKINS, L.D.S. R.C.S., H.D.D.
An indispensable book for students preparing for the F.D.S. and other higher dental examinations. In preparation. *Price*, 30*s. net.*

Order now from all Medical Booksellers or direct from the Publishers

SYLVIRO PUBLICATIONS LTD.
19, WELBECK STREET LONDON, W.1

INTERNATIONAL JOURNAL OF SEXOLOGY

Managing Editor: A. P. PILLAY
Editor for Great Britain: CYRIL BIBBY

Quarterly Vol. 2, No. 3 February 1949

Principal contents:

LEONARD H. BISKIND. Sex and Marriage

W. E. AGAR. Sex Linked Inheritance

VERA I. KRIEGER. The Significance of the Rh Factor for Mother and Child

WALTER SCHINDLER. The Problem of Masochism in Individuals and Nations

C. VAN EMDE BOAS. Coitus Difficulties (Pseudovaginism) Caused by a Variation of the Symphysis

MEYER BARASH. The Social Adjustments of Married Students

Notes—Correspondence—Reviews—Abstracts—etc.

Single copy, 6s. Annual subscription, 22s.

Further details on request from subscription agents:

THE BIOTECHNIC PRESS LTD
BCM/BIOTECHNIC, LONDON W.C.1

HENRY KIMPTON'S PUBLICATIONS

SURGICAL TECHNIQUE
By **A. V. PARTIPILO**, M.D., F.A.C.S.
Fourth Edition | Large Octavo | 676 Pages with 541 Illustrations | Cloth | Price **75s. net**

COLLATERAL CIRCULATION (Anatomical Aspects)
By **DANIEL P. QUIRING**, Ph.D.
Demy Octavo | 142 Pages | 61 Illustrations, 46 Coloured | Cloth | Price **25s.** net (postage 8d.)

ATHLETIC INJURIES
By **A. THORNDIKE**, M.D.
Third Edition | 243 Pages | 114 Illustrations | Cloth | Price **18s** net (postage 9d.)

THE MANAGEMENT OF BINOCULAR IMBALANCE
By **EMANUEL KRIMSKY**, M.D.
Royal Octavo | 464 Pages, with 200 Illustrations | Cloth | Price **63s.** net

OCULAR SIGNS IN SLIT-LAMP MICROSCOPY
By **JAMES HAMILTON DOGGART**, M.A., M.D., F.R.C.S.
Royal Octavo | 126 Pages, with 93 Illustrations, including 85 in Colour | Cloth | Price **21s.** net (postage 9d.)

PRACTICE OF ALLERGY
By **WARREN T. VAUGHAN**, M.D.
Revised by J. HARVEY BLACK, M.D.
Second Edition | Royal Octavo | 1092 Pages | 319 Illustrations | Cloth | Price **75s.** net

THE THERAPY OF THE NEUROSES AND PSYCHOSES
By **S. H. KRAINES**, M.D.
Third Edition | Royal Octavo | 642 Pages | Cloth | Price **32s. 6d.** net (postage 9d.)

DISEASES OF THE ADRENALS
By **LOUIS J. SOFFER**, M.D.
Second Edition | 320 Pages | 45 Illustrations and 3 Coloured Plates | Cloth | Price **32s. 6d.** net (postage 9d.)

REFRACTION OF THE EYE
By **ALFRED COWAN**, M.D.
Third Edition, Revised | Royal Octavo | 287 Pages, with 187 Illustrations and 3 Plates in Colour | Cloth | Price **27s. 6d.** net (postage 9d.)

PRE-OPERATIVE AND POST-OPERATIVE CARE OF SURGICAL PATIENTS
By **HUGH C. ILGENFRITZ**, M.D.
Demy Octavo | 898 Pages | 110 Illustrations | Cloth | Price **52s. 6d. net**

DISEASES AFFECTING THE VULVA
By **ELIZABETH HUNT**, M.D., Ch.B.
Third Edition, Revised | Royal Octavo | 212 Pages, with 36 Illustrations and 19 Coloured Plates | Cloth | Price **25s.** net (postage 9d.)

25 Bloomsbury Way HENRY KIMPTON London, W.C.1
Medical Book Department of Hirschfeld Brothers Ltd.

Digitized by Google

APRIL 2, 1949 PAGES 553 TO 592

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6553 LONDON: SATURDAY, APRIL 2, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

The Rôle and Value of the Anamnesis
Sir ADOLPHE ABRAHAMS, F.R.C.P. ... 553
Retinal and Vascular Damage in Long-standing Diabetes
J. H. CROOM, F.R.C.P.E.
G. I. SCOTT, F.R.C.S.E. ... 555
Deaths from Vagal Inhibition
KEITH SIMPSON, M.D. ... 558
The Adrenolytic Action of Dihydroergocornine in Man
Prof. R. H. GOETZ, M.D.
A. KATZ, M.B. ... 560
Reablement of Tuberculous Patients
R. GRENVILLE-MATHERS, M.R.C.P. ... 563
Cretinism with Goitre in Infancy
VICTORIA SMALLPEICE, M.R.C.P. ... 565

SPECIAL ARTICLES

Convalescent Homes: the Need for Modernisation
Sir HENRY TIDY, F.R.C.P. ... 577
Paludrine in Malaria ... 578
Remuneration in Health Service 579

MEDICAL SOCIETIES

Royal Society of Medicine: Specialisation ... 568

REVIEWS OF BOOKS

Bacterial and Virus Diseases. H. J. Parish, M.D. ... 569
Cytologie sanguine, normale et pathologique. M. Bessis ... 569
Religion and Psychotherapy. A. G. Ikin, M.A. ... 569
The Hormones. G. Pincus, K. V. Thimann ... 569
Introduction to Clinical Orbitonometry. A. C. Copper, M.D. ... 570
The Digestive Tract in Roentgenology. Jacob Buckstein, M.D. ... 570
Modern Trends in Diagnostic Radiology. J. W. McLaren, M.R.C.S. ... 570

LEADING ARTICLES

THE GENERAL PRACTITIONER ... 571
SURGERY OF MITRAL STENOSIS ... 572
MANAGEMENT OF PARKINSONISM 572
1899–1949 ... 573

ANNOTATIONS

Long-term Anticoagulant Therapy ... 574
Pharmacological Aids in Psychiatry ... 574
Training of Health Visitors ... 574
Undecylenic Acid in Psoriasis ... 575
The Estimates ... 575
The Pattern of Disease in Infants' Hospitals ... 576
Sarcoidosis of the Nervous System ... 576
Synthesis of Chloromycetin ... 576

MEDICINE AND THE LAW

Surgeon's Successful Appeal ... 586
Gestation Period and Legal Inferences ... 586

LETTERS TO THE EDITOR

University Remuneration (Mr. G. D. Matthew, F.R.C.S.E.) ... 581
Hæmoglobinuria (Dr. A. Piney) 581
The Undescended Testicle (Dr. S. L. Simpson) ... 581
Opticians and Pharmacists (Mr. A. G. Shaw, PH.C.) ... 581
Vitamin B_{12} (Dr. W. P. Murphy) 581
The Eosinophil Cell (Dr. J. Lendvai) ... 582
Road Accidents (Dr. B. Sandler) 582
Myasthenia Gravis ... 582
On Getting Warm (Mr. R. D. Mothersole, F.R.C.S.) ... 583
Hospital Admissions (Dr. J. M. Greenwood) ... 583
Estimation of Diamidines in Body Fluids (Miss H. Trought, B.SC.) 583
Artificial Insemination (Dr. Robert Forbes) ... 583
Medical Education (Dr. John Plesch) ... 584
Systolic Murmurs ... 584
Crash Helmets (Mr. A. P. Bertwistle, F.R.C.S.E.) ... 584
Coronary Thrombosis (Dr. L. V. Snowman) ... 585
Health Centres (Dr. P. A. Tyser) 585
Exchange Control Medical Advisory Committee (Mr. Walter Elliot, F.R.C.P., M.P.) 585
Specialist Appointments ... 585

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents ... 580

PUBLIC HEALTH

Mineral Oil in Food ... 586
Influenza ... 587
Cooling of Ice-cream ... 587

PARLIAMENT

Question Time ... 587

OBITUARY

William Johnson ... 589
Thomas Morrison Clayton ... 589
John Weir West ... 589
John Richard Tarrant Conner ... 590
George Morris Stoker ... 590

NOTES AND NEWS

Pattern of Our Health Services ... 591
Analgesia in Childbirth in London ... 591
The Belsen Trial ... 591
Scorpion Stings ... 591
Whitaker ... 591
Release of Doctors from Services 591

University of Cambridge ... 591
University of Dublin ... 591
Society of Apothecaries of London 592
Blood Donors ... 592
Royal Society of Edinburgh ... 592
British Orthopædic Association ... 592

Diary of the Week ... 590
Births, Marriages, and Deaths ... 592

'VIBELAN'

Vitamin B Compound B.D.H.

Lassitude and debility are frequently associated with vitamin 'B' deficiency. Four 'Vibelan' tablets daily assist in preventing mental and physical fatigue, help to regularise bowel function and to stimulate appetite. Bottles of 50 tablets.

Literature available on request

THE BRITISH DRUG HOUSES LTD. LONDON N.1

Digitized by Google

OXFORD MEDICAL PUBLICATIONS

THE NATURAL HISTORY OF DISEASE

by JOHN A. RYLE, *M.D., F.R.C.P.*
Professor of Social Medicine in the University of Oxford; Consulting Physician to Guy's Hospital, London, and the Radcliffe Infirmary, Oxford

'Shows medicine as a human art, not to be practised without sympathy and imagination.'—*Lancet*

Second Edition 498 pages 9 illustrations 22s. 6d. net

A PRACTICAL TEXTBOOK OF LEPROSY

by R. G. COCHRANE, *M.D., Ch.B., F.R.C.P., D.T.M. & H.*
Director of the Christian Medical College, Vellore, S. India
With a Foreword by Sir GEORGE McROBERT, *C.I.E., M.D., F.R.C.P., D.T.M. & H.*

'There is no book on leprosy in the English language that is more up to date, practical and better illustrated.'—*British Journal of Dermatology and Syphilis*

296 pages 175 illustrations (1 in colour) 42s. net

SENSORY MECHANISMS OF THE RETINA

With an Appendix on Electroretinography

by RAGNAR GRANIT, *M.D.*
Director of the Nobel Institute for Neurophysiology; Professor of Neurophysiology, Karolinska Institutet, Stockholm

'A crystalization of views and, in addition, an extensive digest of the author's own experimental work.'—*British Medical Bulletin*

436 pages 178 illustrations 35s. net

OXFORD UNIVERSITY PRESS

BRITISH JOURNAL OF UROLOGY

★

Commencing with the March issue (Vol. XXI, Part I) important changes are announced, namely :—

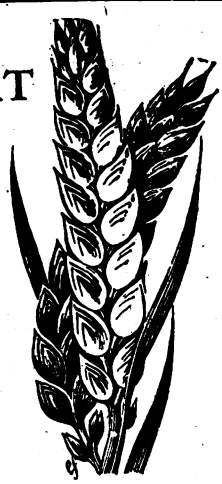
1. A new Editor—**Mr. DAVID BAND**, F.R.C.S. Ed., and two new Assistant Editors—**Mr. J. D. FERGUSSON**, F.R.C.S., and **Mr. N. M. MATHESON**, F.R.C.S.
2. A new Subscription Price—**£2 2s.** yearly (4 issues).
3. A new Publisher—
   E. & S. LIVINGSTONE, LTD.
   16-17, Teviot Place, Edinburgh

*Up-to-date articles by eminent authorities.

*Will be printed on art paper and profusely illustrated.

*The Publishers will be pleased to send a copy of the first issue 'On Approval' to anyone interested.

GREEN CORN AT HARVEST TIME



EVERY practising physician has observed the increase in what may be termed "the cult of sub-normal health"—particularly among young girls.

Usually the positive signs are few. They may well be psychogenic.

If the presenting symptoms are debility, with lethargy, constipation, lustreless hair, adenoids and catarrhal disorders an iodine-deficient thyroid should come high on the list of differential diagnoses.

Adequate iodine intake even in known goitre areas would be assured by the addition of iodine to table salt, as recommended by a subcommittee of the Medical Research Council. Medical men are invited to write for WORLD GOITRE SURVEY, which presents a summary of world knowledge on the use of iodine in the treatment of goitre and its allied conditions. WORLD GOITRE SURVEY will be sent free of charge to any interested medical practitioner.

Iodine Educational Bureau
20 STONE HOUSE, BISHOPSGATE, LONDON, E.C.2

Digitized by Google

APRIL 9, 1949 PAGES 593 TO 636

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6554 LONDON: SATURDAY, APRIL 9, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Treatment of Congestive Heart-failure
H. A. REID, M.R.C.P.E.
WILLIAM HUGHES, M.R.C.P... 593

Subcutaneous Implantation of Insulin in Diabetes Mellitus
Prof. LUIS VARGAS, M.D..... 598

Complete Rupture of the Membranous Urethra
A. H. HUNT, F.R.C.S.
C. NAUNTON MORGAN, F.R.C.S. 601

Filamentous Forms Associated with Newly Isolated Influenza Virus
C. M. CHU, M.B.
I. M. DAWSON, PH.D.
W. J. ELFORD, PH.D..... 602

Rôle of Di-isopropyl Fluorophosphonate in Surgery
J. P. QUILLIAM, M.B.
T. A. QUILLIAM, M.B..... 603

Operation for Severe Varicose Veins During Pregnancy
HAROLD DODD, F.R.C.S..... 606

Mortality from Pink Disease in 1923–47
W. P. D. LOGAN, M.D..... 608

SPECIAL ARTICLES

Intravenous Procaine
W. W. MUSHIN, M.B.
L. RENDELL-BAKER, M.B.... 619

The Problem of Home Accidents 620

New Zealand Hospital Salaries.. 622

NEW INVENTIONS

Suspension Bar for the Davis Gag
BRIAN REEVES, F.R.C.S.E. .. 610

MEDICAL SOCIETIES

Royal Society of Medicine: Carcinoma of the Breast..... 610

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents ... 624

LEADING ARTICLES

VIRUS FILAMENTS 613

SEX HORMONES IN MAMMARY CANCER 613

IMPLANTATION OF INSULIN..... 614

MEASURES OF MORBIDITY..... 615

ANNOTATIONS

British Medical Guild 616

An Epidemic of Thyrotoxicosis.. 617

Transmission of Light Through Skin 617

Streptomycin in Tuberculous Meningitis 618

Continued Care at Cambridge.... 618

The King's Health..... 618

DISABILITIES

27. Paroxysmal Auricular Fibrillation 623

LETTERS TO THE EDITOR

The Royal Colleges (Dr. W. A. Bourne)..... 625

Toxicity of Tridione (Dr. C. W. M. Whitty)..... 625

Oxygen Therapy in Shock (Dr. H. Z. Scheuring) 625

Female Circumcision in the Sudan (Lady Huddleston) 626

Health Centres Now? (Dr. J. W. Nicholas)..... 626

Persistent Malarial Infestation in Fully Mepacrinised Troops (Dr. P. D. Bedford)..... 627

Specialist Salaries (Mr. Derek Jefferiss, M.R.C.O.G.)..... 627

Tuberculous Abscess at the Site of Penicillin Injections (Dr. S. D. Elek) 628

Strangulated Hernia Treated by Native Enterostomy (Dr. M. P. Browne, Dr. B. B. Waddy).... 628

At the Cross-roads..... 628

The Undescended Testicle (Dr. A. W. Spence)..... 628

Cardiospasm (Dr. A. P. Magonet) 629

Cancer of the Breast (Mr. H. J. B. Atkins, F.R.C.S.; Mr. C. C. Holman, F.R.C.S.)..... 629

REVIEWS OF BOOKS

Textbook of Genito-Urinary Surgery. H. P. Winsbury-White, F.R.C.S. 611

The Thyroid and its Diseases. Prof. J. H. Means..... 611

Psychoanalysis Today. Sandor Lorand, M.D..... 611

Physical Aspects of Colour. P. J. Bouma 611

Physics and the Surgeon. H. S. Souttar, F.R.C.S..... 612

Ocular Signs in Slit-lamp Microscopy. J. H. DOGGART, F.R.C.S. 612

PARLIAMENT

Red Cross Aid for Arab Refugees 630

Question Time: Provision of Analgesic Apparatus — Analgesia in Scotland—Emergency Beds—Spa Treatment..... 630

PUBLIC HEALTH

Fluorosis at Fort William 632

Statistics for 1948 633

B.C.G. Trials..... 634

Smallpox 634

Influenza 634

Notification of Infectious Diseases 634

OBITUARY

Philip Bruce White 634

NOTES AND NEWS

Living in Communities 635

Sugars and Bacteria 635

A Surgeon's Story 635

University of Leeds..... 635

University of Aberdeen..... 635

Royal College of Physicians of London 635

Royal College of Surgeons of England..... 635

Royal College of Surgeons in Ireland..... 635

Diary of the Week..... 636

Births, Marriages, and Deaths... 636

From Baillière's Book List

PAPERS ON PSYCHO-ANALYSIS

By ERNEST JONES, M.D., M.R.C.P., President of the International Psycho-Analytical Association and Honorary President of the British Psycho-Analytical Society.
5th Ed. Pp. viii + 504. **31s. 6d.**
"Recommended not only to the specialist but to the medical man who wants an authoritative exposition of psycho-analytical teaching." —*The Lancet*

MYCOSES AND PRACTICAL MYCOLOGY

By N. GOHAR, M.R.C.S. (Eng.), and L.R.C.P. (Lond.), Assistant Professor, Parasitology and Mycology, Fouad I University, Cairo.
Pp. xi + 234. 4 Colour Plates, 134 Illustrations and Diagrams. **25s.**
A concise clinical and practical guide to mycotic infections intended for the dermatologist, general practitioner and student of tropical medicine.

ELEMENTARY ANÆSTHESIA

By W. N. KEMP, M.D., C.M., Consultant Anæsthetist, Children's Hospital, Vancouver, B.C.
Pp. xi + 289. Over 100 photographs, drawings and diagrams. **27s. 6d.**
A complete work on the subject. Discusses in detail all the methods and equipment of general and regional anæsthesia in common usage.

BRONCHIOGENIC CARCINOMA

(AND ADENOMA) By B. M. FRIED, M.D., Associate Attending Physician, Montefiore Hospital.
Pp. 250. 118 Illustrations. **33s.**
Dr. Fried's book based on extensive clinical and post-mortem material makes a valuable contribution towards early diagnosis and treatment. Both primary and metastatic carcinoma are considered as well as bronchiogenic adenoma and tumours of the mediastinum.

BAILLIÈRE, TINDALL AND COX, 7-8 HENRIETTA STREET, COVENT GARDEN, W.C.2

Digitized by Google

PYLOSTROPIN

TRADE MARK

LAMELLAE ATROPINE METHYL NITRATE 1/750 gr.

For the treatment of

PYLORIC STENOSIS

in Infancy

•

Recommended as most suitable for home administration by the mother, each Lamella contains the equivalent approximately of 1 c.c. Atropine Methyl Nitrate solution 1 in 10,000

IN CARTONS OF 42 LAMELLAE

A product of

CLAY & ABRAHAM LTD

Manufacturing Chemists, LIVERPOOL, 1

ESTABLISHED 1813

CA 147

Pyogenic Infections of the Skin

A Public Analyst Reports:—

"The Agar Plate tests indicate the superiority of Valderma over the other ointments, when used to inhibit the growth of B coli, B. megatherium, or Staph. albus. Cultures of Strep. faecalis are translucent and do not photograph well, but visual observation showed that the effect was similar.

There has certainly been a genuine effort to produce a medicament for the skin, which will be antiseptic, when applied, and, will tend to kill organisms on the skin, and to inhibit the growth of mild bacterial infections. In my opinion this effort has been highly successful."

The above is an extract from the report by a Public Analyst of his findings as a result of a series of bacteriological tests by the United States Food and Drug Administration Methods of Testing Antiseptics and Disinfectants. Complete data will be forwarded to any Doctor who may be interested to see them. Write to Dae Health Laboratories, Research Division, 26, Berners Street, London, W.1.

Valderma *oil-in-water emulsion base*

THE SAFE LAXATIVE

Constipation is a common cause of ill-health, and it is the concern of those who tend the sick to relieve their patients from this disorder.

In this connection, 'California Syrup of Figs' perfectly meets the need for a safe yet efficacious aperient. Completely void of mineral or synthetic cathartics, it is corrective not purgative, and re-educates the bowel to normal function.

Its pleasant taste and simplicity of dosage makes 'California Syrup of Figs' the laxative of choice for young and old alike.

'CALIFORNIA SYRUP OF FIGS'

1, WARPLE WAY, LONDON, W.3

Digitized by Google

APRIL 16, 1949 PAGES 637 TO 676

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6555 LONDON: SATURDAY, APRIL 16, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Wertheim's Operation in Retrospect — VICTOR BONNEY, F.R.C.O.G.. 637

Excretion of Chloride and Sodium after Surgical Operations — A. W. WILKINSON, F.R.C.S.E. B. H. BILLING, B.A. GABRIELLA NAGY, B.SC. C. P. STEWART, M.SC..... 640

Treatment of a Stammerer in the Secondary Stage of Stammering — M. C. CRICKMAY..... 644

Factors Influencing the Maintenance of Antitoxic Immunity — MOLLIE BARR, M.SC. A. T. GLENNY, B.SC., F.R.S.... 646

Intestinal Rupture following Non-penetrating Injury — GEOFFREY FLAVELL, F.R.C.S. 649

Gynæcomastia during Treatment with Amphetamine — P. H. TOOLEY, M.R.C.P., CHRISTOFER LACK, M.R.C.S... 650

Fibrocystic Disease of the Pancreas in an Infant — G. G. JONES, M.R.C.S..... 651

Estimation of Ergothioneine in Urine by Paper Partition Chromatography — ELIZABETH WORK, PH.D.... 652

SPECIAL ARTICLES

Studies of Child Growth in the United States — J. M. TANNER, M.D..... 663

Malignant Disease of Female Pelvic Organs..... 665

The Block and the Study-day ... 666

Regional Hospital Boards..... 667

MEDICAL SOCIETIES

Ophthalmological Society of the United Kingdom..... 654

LEADING ARTICLES

CRYPTOGRAM OF AGE..... 657

COLD AGGLUTININS..... 657

TOXICITY OF NEW INSECTICIDES 658

THE BUDGET AND THE N.H.S.. 659

ANNOTATIONS

A Venous Shunt for Mitral Stenosis..... 660

Child and Youth Welfare throughout the World..... 660

The Severely Disabled Adolescent 661

Treatment of Uræmia..... 661

Diet and Dental Caries..... 662

PARLIAMENT

Paying for our Social Services .. 672

Question Time: Eradication of Bovine Tuberculosis — Composition of National Flour — Provision of Analgesia..... 673

LETTERS TO THE EDITOR

The General Practitioner (Dr. J. S. Taylor; Dr. C. H. Watts; Dr. G. A. Ballance).. 669

Benadryl in Parkinsonism (Dr. E. A. Gates)..... 670

Clinical Estimation of Basal Metabolic Rate (Dr. Eugene Bene)..... 670

Liver Extracts (Mr. J. B. M. Coppock, PH.D.; Dr. H. M. Walker)..... 671

Medical Treatment Abroad (Dr. B. G. Edelston)..... 672

The Eosinophil Cell (Dr. F. Duran-Jorda)..... 672

Road Accidents (Dr. H. R. E. Wallis)..... 672

REVIEWS OF BOOKS

Ernährungslehre und Diätetik. M. J. Demole and others..... 655

The Nomenclature of Disease... 656

Some Common Psychosomatic Manifestations. J. B. Murray, M.R.C.P..... 656

Hematology. Prof. C. C. Sturgis, M.D..... 656

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents... 668

PUBLIC HEALTH

Mineral Oil in Food..... 675

OBITUARY

Gilbert William de Poulton Nicholson..... 674

Arthur Hedley Clarence Visick.. 674

NEWS

University of London..... 675

University of Edinburgh..... 675

University of St. Andrews..... 675

Royal College of Surgeons of England..... 675

Royal College of Physicians of Ireland..... 676

Royal Faculty of Physicians and Surgeons of Glasgow..... 676

Royal College of Obstetricians and Gynæcologists..... 676

British Hospitals Association.... 676

Almroth Wright Lectures..... 675

British Association..... 676

Seminological Centre..... 676

Hospital Honours its Staff..... 676

Congress of Catholic Doctors.... 676

Diary of the Week..... 676

Appointments..... 676

Births, Marriages, and Deaths... 676

Demy 8vo 298 + x pages Illustrated 15s., plus 5d. postage

ENDOCRINE DISORDERS IN CHILDHOOD AND ADOLESCENCE

By H. S. LE MARQUAND, M.D. (Lond.), F.R.C.P. (Lond.), Physician, Royal Berkshire Hospital, and F. H. W. TOZER, M.D. (Lond.), M.R.C.P. (Lond.), Sometime Clinical Assistant, Royal Berkshire Hospital

HODDER & STOUGHTON LTD. 20, WARWICK SQUARE, LONDON, E.C.4

Digitized by Google

OXFORD MEDICAL

PUBLICATIONS

KAYNE, PAGEL, AND O'SHAUGHNESSY'S PULMONARY TUBERCULOSIS

Pathology, Diagnosis, Management and Prevention

Revised and partly rewritten by

WALTER PAGEL, *M.D.*
Pathologist, Central Middlesex County Hospital

F. A. H. SIMMONDS, *M.D., D.P.H.*
Medical Director, Clare Hall County Hospital, Middlesex

N. MACDONALD, *M.B., M.R.C.P.*
Physician to the Chest Clinic, Redhill County Hospital, Middlesex

L. FATTI, *F.R.C.S.*
Thoracic Surgeon, Hillingdon County Hospital and Harefield County Hospital, Middlesex

SECOND EDITION 738 pages 288 illustrations **63s. net**

SOME COMMON PSYCHOSOMATIC MANIFESTATIONS

by J. BARRIE MURRAY, *M.D., M.R.C.P.*
Diagnostic Physician, Tavistock Clinic; Physician to Bolingbroke Hospital and the Margaret Street Hospital for Diseases of the Chest, London

114 pages **7s. 6d. net**

PSYCHOTHERAPY: ITS USES AND LIMITATIONS

by D. R. ALLISON, *M.D., M.R.C.P.*
Physician to Stockport Infirmary
and
R. G. GORDON, *M.D., D.Sc., F.R.C.P.*
Consulting Neurologist to Stoke Park Colony

168 pages **8s. 6d. net**

MANAGEMENT IN OBSTETRICS

by ANDREW M. CLAYE, *M.D., F.R.C.S., F.R.C.O.G.*
Professor of Gynæcology and Obstetrics in the University of Leeds

196 pages 17 illustrations **12s. 6d. net**

THE BACKGROUND OF THERAPEUTICS

by J. HAROLD BURN, *M.D., F.R.S.*
Professor of Pharmacology in the University of Oxford

376 pages 59 illustrations 26 tables **22s. 6d. net**

A PRACTICAL MANUAL OF DISEASES OF THE CHEST

by MAURICE DAVIDSON, *M.D., F.R.C.P.*
Physician to the Brompton Hospital for Consumption and Diseases of the Chest: Associate Physician to the Royal Cancer Hospital

THIRD EDITION 686 pages 281 illustrations **50s. net**

OXFORD UNIVERSITY PRESS

Digitized by Google

APRIL 23, 1949 PAGES 677 TO 718

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6556 LONDON: SATURDAY, APRIL 23, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Reorientations in Neurology
Sir CHARLES SYMONDS, F.R.C.P. ... 677

Effect of Diethylstilbœstrol on Urinary Excretion of Pregnanediol and Endogenous Œstrogen during Pregnancy
I. F. SOMMERVILLE, M.B.
Prof. G. F. MARRIAN, D.SC., F.R.S.
B. E. CLAYTON, M.B. ... 680

Idiopathic Renal Acidosis in an Infant with Excessive Loss of Bicarbonate in the Urine
THOMAS STAPLETON, M.R.C.P. 683

Preparation and Standardisation of Saccharated Iron Oxide for Intravenous Administration
J. A. NISSIM, M.B.
J. M. ROBSON, M.D. ... 686

Another Case of Louping-ill in Man
E. G. BREWIS, M.R.C.P.
CHARLES NEUBAUER, M.D.
E. WESTON HURST, F.R.C.P. 689

Water-soluble Vitamin K in the Newborn
R. R. GORDON, M.R.C.P. ... 692

SPECIAL ARTICLES

The Scope of the Medical Illustrator
SYLVIA TREADGOLD ... 701

The Hebrew University Hadassah Medical School
ELI DAVIS, M.R.C.P. ... 704

British Medical Students' Association ... 705

PUBLIC HEALTH

Respiratory Mortality and Morbidity in London
G. E. BREEN, M.D.
B. BENJAMIN, B.SC. ... 714

Smallpox in England and Wales 714

Population Estimates for 1948 ... 714

DISABILITIES

28. Fractured Spine ... 705

LEADING ARTICLES

ACHIEVEMENTS WITH CHLOROMYCETIN ... 695

THE ELDERLY PRIMIGRAVIDA ... 696

LEAD AND THE RED CELLS ... 697

ANNOTATIONS

The Nurses' Bill ... 698

A Death from Dicoumarol ... 698

Irregular Discharge from Sanatoria ... 699

Encephalopathy following Pertussis Vaccine ... 699

An Inconclusive Inquiry ... 699

Psychomotor Epilepsy ... 700

Coördinating Medical Congresses 700

LETTERS TO THE EDITOR

Liver Extracts (Dr. D. L. Mollin; Dr. C. C. Ungley) ... 708

Wertheim's Operation (Mr. John Stallworthy, F.R.C.S.) ... 708

Deaths from Vagal Inhibition (Dr. R. B. Hawes) ... 709

Cardiospasm (Mr. E. Watson-Williams, F.R.C.S.E.) ... 709

Tuberculous Abscess at the Site of Injections (Dr. A. G. Hounslow) 709

The Undescended Testicle (Mr. Denis Browne, F.R.C.S.) ... 709

Training of Health Visitors (Dr. E. D. Irvine) ... 710

Coronary Thrombosis (Dr. H. Josephs) ... 710

Specialist Qualifications (Lieut.-Colonel R. L. H. Minchin, M.D.) 710

At the Cross-roads (Dr. A. L. Banks) ... 711

Congestive Heart-failure (Mr. L. Cosin, F.R.C.S.) ... 711

Clinical Estimation of Basal Metabolic Rate (Dr. Raymond Greene) ... 711

Retropubic Prostatectomy (Mr. Terence Millin, F.R.C.S., Mr. C. L. O. Macalister, F.R.C.S.E.) 711

Kwashiorkor (Dr. C. D. Williams) 711

Fibrocystic Disease of the Pancreas (Dr. W. J. Matheson) 712

Resistance to Proguanil (Dr. H. E. M. Kay) ... 712

REVIEWS OF BOOKS

Penicillin and other Antibiotics. G. W. S. Andrews, M.B., J. Miller, B.SC. ... 693

Treatise on Surgical Infections. Prof. F. L. Meleney, M.D. ... 693

Practical Aspects of Thyroid Disease. George Crile, jun., F.A.C.S. 693

Studies of Chronic Pyelonephritis with Special Reference to the Kidney Function. Flemming Raaschou ... 694

Experimental Immunochemistry. Prof. E. A. Kabat, PH.D., Prof. M. M. Mayer, PH.D. ... 694

PARLIAMENT

The Budget Debate Continued ... 712

Medical Care for Foreign Visitors 713

Question Time ... 713

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents ... 707

OBITUARY

Donald George Hall ... 715

Maurice Sorsby ... 715

Felix d'Herelle ... 715

NOTES AND NEWS

Regional Organisation of Ministry of Health ... 716

Three in a Line ... 716

Toxicity of New Insecticides ... 717

Maternity Benefit ... 717

Linctus Diamorphinæ ... 717

An Appointment Terminated ... 717

Poisons Rules and List ... 717

University of Oxford ... 717

National University of Ireland ... 717

University of London ... 717

University of Leeds ... 717

Royal College of Obstetricians and Gynæcologists ... 717

Society of Apothecaries of London 718

London County Medical Society ... 718

Diary of the Week ... 718

Appointments ... 716

Births, Marriages, and Deaths ... 716

PENICILLIN: ITS PROPERTIES, USES AND PREPARATIONS

Deals with Manufacture, Chemistry, Stability, Standards, Pharmacology, Clinical Use, Pharmaceutical Preparations and Legal Aspects

Pp. 199 Illustrated Price 10s. 6d. (postage 6d.)

"Seldom has so much information been compressed into two hundred pages . . ."—THE LANCET

EXTRA PHARMACOPŒIA (MARTINDALE)

In two volumes 22nd edition

Vol. 1. (1941) Pp. 1289. For the Clinician.

Vol. 2. (1943) Pp. 1217. For the Biochemist and Pathologist.

Price per volume 27s. 6d. (postage: 1 vol. 9d., 2 vols. 11d.)

THE PHARMACEUTICAL PRESS, 17, BLOOMSBURY SQUARE, W.C.1

Publishers of the British Pharmaceutical Codex

Digitized by Google

BUTTERWORTHS

MODERN PRACTICE SERIES

These books are for the guidance of general practitioners and advanced students. The subject matter is written by eminent authorities and edited by outstanding specialists.

MODERN PRACTICE IN PSYCHOLOGICAL MEDICINE

Just Published. Edited by J. R. REES, C.B.E., M.A., M.D., F.R.C.P., Honorary Physician (formerly Medical Director), Tavistock Clinic, London; Honorary Consultant Psychiatrist to the Army. In this new work no attempt has been made to elaborate upon the more abstruse aspects of the subject, so that the book gives a complete survey which is essentially practical. Pp. xii + 475 + Index. Price 50s., by post 1s. 6d. extra.

Further titles in this Series, which are in preparation, include:

DERMATOLOGY. Edited by G. B. MITCHELL-HEGGS, O.B.E., M.D., F.R.C.P.
ESSENTIALS OF ANAESTHESIA. Edited by FRANKIS T. EVANS, M.B., B.S., F.F.A. R.C.S., D.A.
DISEASES OF THE EAR, NOSE AND THROAT. Edited by W. G. SCOTT-BROWN, C.V.O., M.D., F.R.C.S.
OPHTHALMOLOGY. Edited by H. B. STALLARD, M.B.E., M.D., F.R.C.S.

A complete illustrated Catalogue, giving fuller information, is available on application to the Publishers.

BUTTERWORTH & Co. (Publishers) LTD., BELL YARD, TEMPLE BAR, WC2

FOR THE BUSY PRACTITIONER

The convenience of tablet medication is undoubtedly of marked value in the treatment of many conditions presented daily to the physician.

This is particularly true of alkaline therapy, where 'Milk of Magnesia' Tablets are a frequent and everyday prescription. In the busy dispensary, or for providing immediate symptomatic relief while visiting the patient's home, they present advantages readily appreciated by the practitioner.

Quickly dispensed, accurate in dosage and convenient to take during working hours, 'Milk of Magnesia' Tablets offer a simple yet efficacious means of combating gastric upset due to hyperchlorhydria.

SPECIAL PROFESSIONAL PACKS

For personal, surgery or dispensing use, a professional pack of 'Milk of Magnesia' Tablets is available. This contains 500 Tablets and costs 10/- (including tax) post free. Orders should be sent direct.

'MILK OF MAGNESIA' TABLETS

THE CHAS. H. PHILLIPS CHEMICAL CO., LTD., 1, WARPLE WAY, LONDON, W.3

★ *'Milk of Magnesia' is the trade mark of Phillips' preparation of magnesia.*

Digitized by Google

APRIL 30, 1949 PAGES 719 TO 762

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6557 LONDON: SATURDAY, APRIL 30, 1949 CCLVI

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Chronic Bronchitis
W. A. LISTER, F.R.C.P. 719
Observations on a Series of Labours
GRANTLY DICK READ, M.D.. 721
Curare-like Actions of Tri-(diethylaminoethoxy)-benzene triethyliodide
W. W. MUSHIN, M.B.
R. WIEN, PH.D.
D. F. J. MASON, B.SC.
G. T. LANGSTON 726
Streptomycin in Non-tuberculous Infections
P. H. BUXTON, M.B.
R. D. SIMON, B.SC.
F. R. SELBIE, M.D..... 729
Experimental Observations on Renal Blood-flow
D. A. K. BLACK, M.R.C.P.
M. G. SAUNDERS, M.B..... 733
Fatal Air Embolism During Blood-transfusion
G. B. DOYLE, M.B.
PATRICIA FRODSHAM, B.M. .. 735
Hæmochromatosis in Three Families and in a Woman
R. D. LAWRENCE, F.R.C.P.... 736

SPECIAL ARTICLES

A Plan for the Aged
C. A. BOUCHER, D.M..... 745
Cardiac Catheterisation
A. J. BENATT, M.D..... 746
Health Programme for the U.S.A. 747
Imperial Cancer Research Fund.. 749

PUBLIC HEALTH

Fever Without Rash after Contact with Smallpox
IAN R. GRAY, M.B..... 749
Smallpox—Influenza..... 751
Births and Deaths..... 751

MEDICAL SOCIETIES

Liverpool Medical Institution and Manchester Medical Society: The Lipoidoses..... 737

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents.... 752

LEADING ARTICLES

ULCERATIVE COLITIS..... 739
CARE OF THE OLD..... 740
VIRUS AND CANCER CELL..... 741

ANNOTATIONS

The Napkin Age..... 742
Leptospirosis in Denmark..... 742
Metopon 743
The International Classification 743
Air Embolism During Transfusion 743
Prevention of Sunburn..... 744
Sex Education for Medical Students 744
Glasses Off the Peg..... 744
Suprarenal Hormone in Rheumatoid Arthritis..... 744

PARLIAMENT

Question Time..... 751

LETTERS TO THE EDITOR

Specialist Appointments..... 753
Operation for Varicose Veins (Dr. S. M. Rivlin) 753
Tuberculous Abscess at the Site of Injections (Dr. G. B. Forbes, Dr. F. G. St. Clair Strange).... 754
German Doctors (Dr. J. P. Dunn) 754
Vitamin B_{12} (Prof. D. M. Dunlop, F.R.C.P., Dr. W. M. Wilson).... 754
Excretion of Chloride and Sodium after Surgical Operations (Dr. J. L. Patton)..... 754
"The Snake Pit" (Dr. E. C. Dax) 754
The General Practitioner's Remuneration (Dr. J. Hopkins) 755
The General Practitioner (Dr. Beryl Harding; Dr. F. Gray).. 755
Intestinal Rupture Following Non-penetrating Injury (Mr. G. E. Moloney, F.R.C.S.E., Mr. J. N. Ward-McQuaid, F.R.C.S.) 756
Health Services Bill in Australia (Mr. Gershon Bennett)..... 756
Wertheim's Operation (Mr. Frank Cook, F.R.C.O.G.)..... 756
Female Circumcision in the Sudan (Dr. A. I. M. Leach)..... 756
Clinical Estimation of Basal Metabolic Rate (Dr. George Discombe) 757
Ergothioneine in Urine (Mr. L. I. Woolf, PH.D.)..... 757
Scorpion Stings (Mr. J. O. Dewey) 757
Benadryl in the Treatment of Parkinsonism (Capt. B. W. Perlow, M.R.C.S.)..... 757
Congestive Heart-failure (Dr. William Hughes)..... 758
Physical Manifestations of Emotional Disorder..... 758
Œsophageal Lesions in Sclerodactyly (Mr. P. R. Allison, F.R.C.S.) 758
Louping-ill (Dr. F. H. Jacob).... 758
Streptomycin in Human Plague (Dr. P. V. Karamchandani).... 758

REVIEWS OF BOOKS

An Atlas of Traumatic Surgery 737
Scientists and Amateurs..... 737
Wuchsstoffe und Antiwuchsstoffe 737
Marriage Crisis 738
Trichomonas Vaginalis and Trichomoniasis 738
Ways to Better Hearing..... 738
Die Überlastungsschäden des Skelettsystems..... 738

OBITUARY

John Ronald Currie..... 759
Howard Bluntisham Hodson.... 759
Charles William Menelaus Hope 759
John Wardle Bone..... 760

NOTES AND NEWS

The National Formulary..... 761
Strengthening the Red Cross.... 761
German Experiments in Water Purification..... 761
International Occasion at Queen Square 761
A Digest of Health Legislation... 761
World Medical Association Bulletin 761
Atomic Bombs..... 761

University of Oxford..... 762
University of Cambridge..... 762
University of London..... 762
University of Sheffield..... 762
University of Birmingham..... 762
University of Bristol..... 762
University of Edinburgh..... 762

Diary of the Week..... 762
Appointments..... 760
Births, Marriages, and Deaths... 760

CHANGING DISCIPLINES

Lectures on the History, Methods and Motives of Social Pathology

by JOHN A. RYLE, *M.D., F.R.C.P.*

Professor of Social Medicine in the University of Oxford; Director of the Institute of Social Medicine, Oxford

'This is a balanced interpretation which illustrates the value and the importance of social medicine for the medical student. It is the best book on the subject which we have yet seen.'—*Bristol Medico-Chirurgical Journal*

138 pages 13 illustrations 10 tables 12s. 6d. net

OXFORD UNIVERSITY PRESS

Digitized by Google

OXFORD MEDICAL PUBLICATIONS

KAYNE, PAGEL, and O'SHAUGHNESSY'S PULMONARY TUBERCULOSIS

Revised and partly rewritten *by* WALTER PAGEL, *M.D.*, F. A. H. SIMMONDS, *M.D.*, *D.P.H.*, N. MACDONALD, *M.B.*, *M.R.C.P.*, and L. FATTI, *F.R.C.S.*

SECOND EDITION — 738 pages — 288 illustrations — 63s. net

SOME COMMON PSYCHOSOMATIC MANIFESTATIONS

by J. BARRIE MURRAY, *M.D.*, *M.R.C.P.*

114 pages — 7s. 6d. net

POST-MORTEM APPEARANCES

by JOAN M. ROSS, *M.D.*, *B.S.*, *M.R.C.S.*, *L.R.C.P.*

FIFTH EDITION — 318 pages — 8s. 6d. net

THE BACKGROUND OF THERAPEUTICS

by J. HAROLD BURN, *M.D.*, *F.R.S.*

376 pages — 59 illustrations — 26 tables — 22s. 6d. net

MANAGEMENT IN OBSTETRICS

by ANDREW M. CLAYE, *M.D.*, *F.R.C.S.*, *F.R.C.O.G.*

196 pages — 17 illustrations — 12s. 6d net

PSYCHOTHERAPY: ITS USES AND LIMITATIONS

by D. R. ALLISON, *M.D.*, *M.R.C.P.*
and
R. G. GORDON, *M.D.*, *D.Sc.*, *F.R.C.P.*

168 pages — 8s. 6d. net

A PRACTICAL MANUAL OF DISEASES OF THE CHEST

by MAURICE DAVIDSON, *M.D.*, *F.R.C.P.*

THIRD EDITION — 686 pages — 281 illustrations — 50s. net

THE PARATHYROID GLANDS AND SKELETON IN RENAL DISEASE

by J. R. GILMOUR, *M.R.C.P.*

172 pages — 26 illustrations — 18s. net

DISEASES OF THE HEART AND CIRCULATION

by A. A. FITZGERALD PEEL, *D.M.*, *F.R.F.P.S.(G.)*

420 pages — 113 illustrations — 35s. net

SENSORY MECHANISMS OF THE RETINA WITH AN APPENDIX ON ELECTRORETINOGRAPHY

by RAGNAR GRANIT, *M.D.*

436 pages — 178 illustrations — 35s. net

HEPARIN IN THE TREATMENT OF THROMBOSIS

by J. ERIK JORPES, *M.D.*

With a Foreword by SIR JAMES LEARMONTH, *K.C.V.O.*, *C.B.E.*, *Ch.M.*, *F.R.C.S.*

SECOND EDITION — 260 pages — 24 illustrations — 18s. net

OXFORD UNIVERSITY PRESS

Digitized by Google

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

RETROPUBIC PROSTATECTOMY

EXPERIENCES BASED ON 757 CASES

TERENCE MILLIN
M.Ch. Dubl., F.R.C.S.
SURGEON

C. L. O. MACALISTER
M.B. St. And., F.R.C.S.E.
LATE SURGICAL REGISTRAR

P. M. KELLY
B. Chir. Camb., F.R.C.S.
SURGICAL REGISTRAR

ALL SAINTS' UROLOGICAL CENTRE, WESTMINSTER HOSPITAL, LONDON

THIS paper is based on an initial series of 757 consecutive cases of retropubic prostatectomy carried out by the senior author and his associates, in private practice and in the various clinics under his care, between Sept. 1, 1945, and Nov. 30, 1948. It includes all cases operated upon by house-officers under instruction. In it we intend to analyse our experiences, good and ill, reiterate our satisfaction with the method, and indicate our hopes for the future.

Since the first publication in this journal in December, 1945, much has been written on the subject both in Europe and America. A number of modifications have been proposed and practised; but, as yet, we remain unconvinced that any major departure from our established technique has proved its worth. It is significant that the majority of surgeons with the greatest experience of the retropubic operations have remained faithful or have reverted, after straying, to all the main points in our procedure.

During the 39-month period under review, 919 cases of prostatic obstruction have been operated upon in our clinics by the following methods:

BENIGN	*Cases*
Retropubic prostatectomy	723
Endoscopic resection (loop or punch)	125
One-stage transvesical prostatectomy (combined with partial cystectomy for atony)	1
Two-stage transvesical prostatectomy	2
Perineal prostatectomy	1
Radical retropubic prostatectomy	1

MALIGNANT	
Endoscopic resection (usually combined with subcapsular orchidectomy)	31
Conservative retropubic prostatectomy	20
Radical retropubic prostatectomy	13
Total cysto-prostatectomy	2

In addition 7 cases underwent subcapsular orchidectomy (without prostatic intervention) owing to œstrogen intolerance.

Analysing the 757 cases who underwent a retropubic operation, they may be thus grouped:

"Adenomatous" or fibroadenomatous	682
Fibrous (i.e., median bar, &c.)	23
Calculous	16
Unsuspected malignancy	20*
Clinically malignant	16†

* 13 of these were not suspect at operation but proved to be carcinomatous on section; 7 were deemed to be carcinomatous at enucleation and the diagnosis ultimately confirmed. In addition, 2 cases, suspect at operation, showed no histological evidence of carcinoma.

† 14 of these underwent a radical prostatectomy and 2 were subjected to transplantation of the ureters and total cystoprostatectomy, owing to extensive bladder base involvement.

The above figures show that our overwhelming preference is for the retropubic approach when dealing with the "enucleable" gland. We reserve the endoscopic route for minor subcervical lobes and the medium-sized glands in the very poor surgical risk. In the latter group, with increasing experience, we are employing the open technique more and more: in our last 200 retropubic operations there have been 12 octogenarians, only 1 of whom died, and during the past twelve months we have carried out 259 retropubic prostatectomies, as against 39 endoscopic resections, for benign obstruction.

FIBROUS PROSTATE

In the fibrous group, a relatively large number were subjected to the open operation, though most authorities agree that the endoscopic technique is satisfactory for such scleroses. To justify our practice we can but say that we have given a reasonably extensive trial to the retropubic operation for this type of case and have not found it wanting. It should be an encouragement to those surgeons called upon to deal with all types of prostatic obstruction who have not mastered the intricacies of the endoscopic route. Most of these fibrous obstructions manifest themselves at a younger age, when a slightly increased operative trauma is of little moment. We ourselves still feel that the operation of choice for most scleroses of the vesical neck is a transurethral resection, provided the surgeon is practised in this technique.

In our 23 cases there have been no deaths. The hospital stay has been but two or three days longer than if the endoscopic route had been employed, the postoperative course little different, the "urethral convalescence" rather speedier, and the ultimate functional results apparently equally good. With a very stout patient we would lean towards the endoscopic route, owing to increased operative difficulties in the retropubic approach to the small gland; but, where the urethra is of small calibre, we would choose the open technique. We shall continue to judge each case on its merits.

CALCULOUS PROSTATITIS

Under this heading we do not include the "adenomatous prostate" which contains multiple calculi in the peripheral subcapsular zone, and which nearly always is best treated by open enucleation, but only the small, sclerotic, infected, calculous prostate which defies digital enucleation owing to the absence of a subcapsular plane of cleavage. Formerly in these cases we advocated a transurethral resection, but in the light of our retropubic experiences, we now prefer the open operation because of its greater completeness and better functional results. In the less infected cases we employ our intracapsular procedure, dissecting out the fibrous nodules with scissors, curetting the residuary calculi, and excising a generous wedge from the sclerotic lip of the vesical outlet; for the more infected glands, and for older men to whom the maintenance of sexual potency matters little, we employ the radical subtotal prostatectomy we have described elsewhere (Millin 1947).

CARCINOMA OF THE PROSTATE

During the period under review, approximately 200 cases, diagnosed as prostatic malignant disease, were seen. Only 16 were deemed suitable for radical surgery. Recently, however, we have been extending the scope of the radical operation by giving one month's œstrogen therapy, and following this by complete retropubic extirpation of prostate, vesicles, and half the bladder base. The immediate results of the radical operation have, on the whole, been gratifying, but it is too early to speak of late results.

Of the cases subjected to this radical intervention all but 1 proved, on microscopy, to be malignant. In the case of mistaken diagnosis the prostate was suspiciously hard on rectal examination and confirmed as such on retropubic palpation, and we were much surprised to find no histological evidence of malignancy on serial section.

In 1 case, complete urinary incontinence followed; but here the malignant process involved the apex of the gland and it was necessary to make the distal section through the mobilised membranous urethra. The patient has had no œstrogen therapy and now eighteen months later, is in excellent health, has put on 20 lb. in weight, and shows no clinical evidence of malignancy. We propose carrying out a urethroplasty to remedy his incontinence.

Digitized by Google

Relatively few carcinomatous prostates present themselves early enough to warrant the radical operation with a hope of cure, but from time to time cases are discovered (either on rectal examination or unexpectedly at operation) in which it seems to be indicated. For these we prefer the retropubic approach to the perineal, because an even more extensive operation can be carried out. There is no limit to the amount of bladder base which can be removed; and, where the ureteric orifices must be sacrificed or jeopardised, the ureters may be implanted higher in the bladder or transplanted into the colon. We hope later to present a follow-up of the cases subjected to the radical operation.

PRELIMINARY INVESTIGATION

In addition to a full clinical survey, bacteriological assay of the urine, and such ancillaries as electrocardiographic study when indicated, we make much use of intravenous urography. This, besides giving an excellent renal function test, reveals any effects of back pressure in the upper tract (dilated ureters or renal pelves); vesical diverticula may be outlined and the approximate residual urine can be assessed. Blood-urea is estimated as a routine. The blood is examined for hæmoglobin content and to rule out dyscrasias; and the blood-group is noted lest transfusion be required.

PREOPERATIVE TREATMENT

For a number of years we, like most urologists, have avoided unnecessary urethral instrumentation. Catheters are never passed merely to ascertain the amount of residual urine. Where there is doubt as to the diagnosis (e.g., the possibility of congestive prostatitis or an intravesical subcervical lobe accounting for symptoms) or where hæmaturia has been a symptom, a preliminary cysto-urethroscopic study must be made. In general, however, the endoscopic examination is made as a preliminary part of the operation, and equipment is ready sterilised for both the retropubic operation and an endoscopic resection.

URETHRAL CATHETER DRAINAGE

In some quarters it is the fashion to avoid urethral catheter drainage like the plague and to urge immediate prostatectomy irrespective of renal function or other tests. Having given this latter method a trial and lost—from rapidly progressive renal failure—2 patients, who might have been saved by less hasty intervention, we have reverted to the use of the indwelling catheter in cases with a chronic retention, particularly if there is clinical evidence of uræmia or suburæmia. In cases of acute retention where the general condition is good and operation is possible within thirty-six hours, we resort to relief by an indwelling suprapubic trochar, using the fine instrument commonly employed for tapping hydroceles. In cases where prompt operation is for any reason impossible, we rely on a tied-in no. 15 Ch. rubber Tiemann or small Foley catheter. Sulpha drugs are routinely given. Comparing fatality-rates and morbidity as evidenced by the postoperative temperature charts and the length of stay in hospital, we find no evidence to support the wholesale use of immediate prostatectomy, nor disastrous results from the indwelling catheter. In general, however, we are employing preliminary drainage rather less frequently than formerly, as is shown by the following figures.

	Cases 300–400	*Cases 600–700*
No preliminary drainage	55	67
Catheter 1–7 days	19	16
„ 7–14 „	13	4
„ 14–21 „	3	2
„ more than 21 days	2	2
Suprapubic cystostomy (5 elsewhere)	8	9 (5 elsewhere)

PRELIMINARY SUPRAPUBIC CYSTOSTOMY

Of the 723 cases of benign prostatic obstruction operated on by the retropubic route, the procedure was secondary in 50 (6·9%). Of these 50, however, 28 had their preliminary suprapubic cystostomy before coming under our care, and some of them might otherwise have had a one-stage operation. We normally employ urethral catheter drainage where some form of decompression is required; but, if the patient's condition does not obviously improve under this form of therapy, or if after 14 days' such drainage prostatectomy is not deemed advisable, we resort to the suprapubic tube. Such is only an approximate rule and exceptions will arise from time to time. One patient remained on indwelling catheter drainage for over five months before operation was agreed to. A second, a medical man, relied on intermittent catheterisation for nine months before he consented to a prostatectomy. Both were successfully dealt with.

TECHNIQUE

The technique of the operation has been sufficiently described elsewhere, but we would stress certain points in our present technique.

We now invariably employ a transverse incision of the skin at the level of the upper border of the pubis. The anterior sheath of the recti is incised in a curve with the convexity downwards, and the "bucket-handle" flap is turned upwards, so exposing the underlying pyramidales and recti. The muscles are separated in the midline. The preprostatic veins, if present, are divided between hæmostats and diathermised. Gauze packs are then placed on each lateral aspect of the gland. This manœuvre, dispensed with by some operators as unnecessary, we regard as very important, because it defines accurately the limits of the prostate and gives full exposure.

The prostate is injected subcapsularly with 20 ml. of 1% procaine solution containing 0·5 ml. 'Pitressin': this opens up the correct plane of cleavage, and seems to minimise operative bleeding and hasten contraction of the prostatic bed after enucleation. Midline stay sutures are placed in the capsule above and below the proposed line of incision. The capsule is always incised transversely 1 cm. below the bladder neck when dealing with the adenomatous prostate and the opening is minimal in length, 2–3 cm. The urethra is deliberately divided with scissors at the distal limits of the lateral lobes, so avoiding any risk of avulsing a portion of the membranous urethra, the commonest cause of persistent incontinence. The lateral lobes are delivered in turn to avoid the risk of unduly enlarging the capsular incision. Wherever there is evidence of sclerosis of the vesical outlet, a wedge is excised from its posterior lip: this is indicated in approximately 75% of cases. Otherwise the apex of the trigone is fixed to the floor of the prostatic bed by a retrigonisation suture of the Harris type. In some cases of pure lateral-lobe hypertrophy each lobe is enucleated in turn, leaving the mucous membrane of the floor of the posterior urethra intact. The prostatic arteries are underpinned with a stitch on each side.

For postoperative drainage we remain faithful to a no. 18 or 20 Ch. Harris type of urethral rubber catheter. It is accurately placed so that both eyes lie within the bladder. Multiple-eyed catheters should, in our view, not be employed, and we do not favour the Foley type for postoperative drainage. (The 24 Ch. Foley commonly used in the United States has all the demerits of such a relatively large catheter, and the added disadvantage of a poorer lumen for drainage than the no. 18 Ch. Harris type.)

The capsular incision must be accurately closed with a continuous stitch; we employ no. 1 chromicised

Digitized by Google

catgut. This suture should effectively control all bleeding from the capsule. Careful inspection is then made to ascertain that there is no ooze from vessels in the pre-prostatic fat. Bleeding points should be underrun with a stitch or diathermised. In rare cases where the oozing is not thus satisfactorily controlled, a light gauze pack may be left in and removed 24 hours later, or alternatively, oxidised cellulose or calcium alginate may be fixed in position. All bleeding must be controlled.

We remove the catheter almost routinely on the third postoperative day. In cases where the capsule has been inadvertently split during enucleation, where doubt exists about the thorough closure of the capsular incision, where the capsule is excessively thin, or where post-operative bleeding is unusually prolonged, we have no hesitation in leaving the catheter in a few days longer.

The operative time should not exceed 20–30 minutes, and the operation should not, in our opinion, be undertaken by those referred to so aptly by Sir Gordon Gordon-Taylor as the "surgical dawdlers." Our operative blood-loss seldom exceeds 160 ml.

Blood-transfusion is rarely necessary. On reviewing 100 consecutive private cases we find that 2 octogenarians were given a preoperative transfusion, and in 3 others blood was administered, after operation, for anæmia caused by unusually prolonged postoperative hæmaturia. In no case in the series was blood administered as an emergency measure for excessive operative blood-loss. The All Saints' Hospital series reveals a similar state. Of 100 consecutive cases only 4 received blood-transfusion after operation.

Considerable misconception seems still to exist as to what is actually seen and accomplished in the retropubic operations. For example, in a recent textbook of urology, the editor suggests that in resecting a wedge from the posterior lip of the vesical outlet the ureteric orifices are in danger; that the technique is unsuitable for the fibrous prostate; and that osteitis pubis and pelvic cellulitis are common complications. Others have said that the operation is difficult and bloody. Such statements can emanate only from those with little experience of the retropubic technique. We would reply that by drawing on the apex of the trigone, after enucleation, the bladder base is well exposed and the ureteric orifices are clearly seen. In answer to the other criticisms, we present the following figures, representing all cases operated upon retropubically by our house-surgeons and registrars at All Saints' Urological Centre during the past two years:

Total cases operated upon	59*	*Age-groups*	50–60 .. 7 cases
			60–70 .. 28 ,,
			70–80 .. 22 ,,
			80–90 .. 2 ,,
Deaths	0		
Osteitis pubis	0		
Pelvic cellulitis	0		

* Not all these cases are included in our 757 cases, for some were operated upon by the junior staff for our colleagues with separate services.

These figures show that the technique can be mastered even by relatively inexperienced urological surgeons, provided they have been adequately trained.

POSTOPERATIVE COMPLICATIONS

In the age-group to which prostate patients belong complications must often arise; but they have been fewer after retropubic operations than with any other technique we have employed. We shall deal with those most frequently met with or spoken about—not always the same thing!

Pelvic Cellulitis

In 757 cases we are aware of only 2 deaths which might be attributed to pelvic cellulitis. (Neither was confirmed by necropsy.) All who have operated on cases shortly after major operations such as Wertheim's hysterectomy will have noticed a tissue reaction which in the presence of even minimal infection would be labelled pathologically "cellulitis." All extraperitoneal operations are followed by such a tissue reaction, and it is only when the bacterial attack is overwhelming and the drainage faulty that the result is fatal. Every care must, of course, be taken to prevent infection before, during, and after operation.

Osteitis Pubis

This troublesome lesion has apparently become more common in recent years. Its symptoms are so obvious that it can scarcely have been missed in the past; yet the senior author can recall but a single instance in 18 years of urological surgery prior to 1946. The literature now abounds with instances of its following all varieties of prostatic surgery. Kirz (1947) in a careful radiological follow-up of 300 cases of suprapubic operations on the prostate and bladder found the surprisingly high incidence of 3%.

In seeking a cause for this apparent increase we naturally thought of new therapeutic agents, such as the sulpha drugs and the antibiotics. In discussing the subject with Mr. Yates Bell, who used penicillin extensively before most urologists in this country, and reported 4 cases of osteitis pubis in a short series of Harris prostatectomies in 1948, we came to the conclusion that the cause might be prompt healing of the superficial wound, with locking up of *Pseudomonas pyocyanea* and other resistant organisms. Accordingly we have now abandoned the routine use of penicillin and employ it only when it appears to be definitely indicated.

Osteitis pubis, though disabling to the patient for several weeks, or in severe cases months, is self-limiting, and we have never seen it lead to osteomyelitis or sequestrum formation. Recovery is complete. We have met with the complication 6 times but in only 3 was it severe.

Suprapubic Fistula

Some reports on the operation, chiefly continental, have mentioned a relatively high incidence of suprapubic urinary leakage on removing the catheter. We routinely remove the catheter on the third or fourth postoperative day, and very seldom see this relatively minor complication. It usually betokens faulty capsular suturing. In our first 400 cases the incidence was 9%, but on reviewing our last 200 benign one-stage operations we have obtained the following figures:

Private cases.. ..	81	with	3	postoperative leaks,	i.e., 3·7%
Voluntary hospital ..	103	,,	5	,, ,, ,,	4·8%
Municipal hospital ..	16	,,	1	,, ,, ,,	12·5%

This represents an average incidence of 4·5%. When it occurs, it is but necessary to replace the catheter for a further few days. We have had no case of persistent fistula.

In our last 57 consecutive cases in the Royal Masonic Hospital there has been not a single case of leakage and no death.

Reactionary Hæmorrhage

Frank hæmaturia is the rule during the first day or two and it demands watchful attention to the catheter drainage. The first sign of faulty drainage of the catheter should call for a small lavage to remove the offending clots. "Keep the bladder empty and the bleeding will automatically stop" is the rule for aftercare. In our complete series we have only once had to perform a suprapubic cystotomy for postoperative bleeding; this was in the 393rd case, thirty-six hours after operation, for retained clot which could not be removed by aspiration through a catheter.

Secondary Hæmorrhage

This has never been of such severity as to demand a cystotomy. We have, of course, seen the complication, as have all operators in prostatic surgery, by whatever

Digitized by Google

route. The catheter must be replaced at the first sign of bright blood in the urine, which is most often seen about the sixth postoperative day. Retention of the catheter for forty-eight hours should suffice. In 2 of our cases repeated secondary hæmorrhages occurred, five and six in number, calling for replacement of the catheter and blood-transfusion. Both patients recovered.

The following figures show the incidence of secondary hæmorrhage, requiring replacement of the catheter, in our last 200 cases:

Group	Cases	Secondary Hæmorrhage	Percentage
Private	81	6	7·4
Voluntary hospital	103	9	8·7
Municipal hospital	16	1	6·3

The average incidence was 8%.

Postoperative Stricture

Before we appreciated the importance of excising a wedge from the posterior lip of the vesical outlet when any sclerosis was present, we encountered this complication 5 times in 75 cases. Since adopting this almost routinely we have seen stenosis of the vesical outlet in only 3 cases out of 675. Of these, 2 required a subsequent endoscopic resection; the other responded to dilatation and the condition was probably merely a mucous-membrane cross-union. We have only once seen stenosis at the distal extremity of the prostatic bed, and it yielded to a few dilatations.

Incontinence

Incontinence has been a persistent phenomenon in only 2 cases. One patient was an octogenarian, and it was difficult to say whether we were dealing with a true sphincteric dysfunction or merely an urgency. The loss was minimal three months later. The other case of lasting incontinence was that mentioned above as a stricture at the distal extremity of the prostatic bed. This responded ultimately to a series of urethral dilatations, and seven months after operation was completely cured.

We should mention that we have seen 4 cases of persistent incontinence following retropubic operations by other surgeons. In all of these we carried out our urethroplasty with success.

Pulmonary Embolus

Pulmonary embolus has been seen 11 times, but it was fatal in only 5 instances, 3 of the deaths being in octogenarians. The 4th case was in an outlying hospital where the patient was kept in bed for ten days and on being lifted out into a chair rapidly developed a massive fatal pulmonary embolus, proved post mortem. The 5th was in a patient who, on the fifteenth day, was packing his bags to leave hospital.

Funiculitis

Despite a routine bilateral vasectomy this complication will develop in a proportion of cases, perhaps more often than in the suprapubic type of operation, owing to the early re-establishment of micturition.

MORTALITY

In the 724 cases of retropubic prostatectomy for benign prostatic obstruction there have been 33 deaths, an over-all fatality-rate of 4·6%.

The figures can be broken down into age-groups as follows:

Age	No.	Deaths	Fatality-rate			
50–60	78	2	2·6%	1·8%		
60–70	361	6	1·7%		2·8%	
70–75	172	9	5·5%			3·9%
75–80	81	10	12·3%			
80–90	32	6	18·8%			4·6%

The figures in the last 200 cases are:

50–70	110	2	1·8%	1·9%		
70–75	49	1	2·0%		3·1%	
75–80	29	3	10·4%			3·5%
80–90	12	1	8·3%			

The steep rise in the fatality-rate at the older ages is not generally appreciated. A comparison of the St. Mark's Hospital figures for excision of the rectum shows a similar state of affairs. The inference is that earlier operation should be advised in established prostatic obstruction, particularly when the retropubic procedure entails such a relatively short stay in hospital.

POSTOPERATIVE HOSPITAL STAY

In an earlier study of 200 consecutive cases, private and hospital, we found an average postoperative stay of 16·2 days. Reviewing the last 100 cases operated upon retropubically in All Saints' Urological Centre—omitting the malignant cases, the deaths, and the two-stage operations—we find that the average stay in the 88 one-stage retropubic prostatectomies for benign prostatic obstruction is 16·4 days.

There were 4 patients who remained in hospital more than six weeks: one, an octogenarian, because his family refused to have him home; a second because of intestinal obstruction due to a volvulus which required operative cure; a third (already mentioned) who developed clot retention necessitating suprapubic cystostomy, and who proceeded to have five subsequent secondary hæmorrhages; the fourth for anaplastic anæmia which finally yielded to appropriate treatment.

Nearly two-thirds (62%) were discharged in fourteen days or less.

SECOND-STAGE RETROPUBIC PROSTATECTOMY

In considering the relative merits of the retropubic technique, after cystostomy, as against the more rapidly performed Freyer enucleation, we must admit that many urological surgeons, who employ the retropubic operation in cases they think fit for a one-stage procedure, prefer the transvesical technique where a cystostomy exists. Our own experiences favour the retropubic technique in most cases in view of the shortened hospital stay, easier and more comfortable postoperative course and approximately parallel fatality-rate.

The average *postoperative stay* in hospital in the 50 cases was 22·6 days. The senior author, reviewing a similar series of his second-stage transvesical enucleations, found that the postoperative hospital stay averaged 31·4 days, and consideration of a similar series of the late Mr. Sydney Macdonald gave an almost identical figure—31·6 days. (These latter series were admittedly before the widespread use of sulpha drugs and antibiotics.)

Fatality-rate.—The series is too small to be of statistical significance; but 2 cases died—both in the municipal hospital group—a mortality-rate of 4%.

MODIFICATIONS

Every surgical operation will be modified by individual operators to suit their own taste. There are, however, certain so-called modifications with which we disagree.

The first is the advocacy of a longitudinal incision in the capsule, in all cases. We ourselves formerly employed this in dealing with the fibrous types of obstruction, but have always condemned it for the larger adenomatous glands. In our experience the bleeding is no less on incising the capsule vertically, for one is dealing with an interlacing venous plexus and not a series of veins coursing cranially parallel to one another. With our present technique and correct armamentarium, the bleeding from the short transverse incision is negligible. We agree that suturing the longitudinal incision will in general be easier, but closing the transverse incision accurately should not be beyond the capabilities of those undertaking this work. The chief objection to the routine use of the vertical incision is that the main bulk of the adenoma is situated posteriorly; and, as the anterior dimensions of the prostate are seldom elongated commensurate with the lateral-lobe enlargement (as seen in the exaggerated posterior curve of the prostatic urethra on urethrography in cases of marked prostatic hypertrophy), there is a real risk of splitting the capsular

Digitized by Google

incision in enucleating a large adenoma. If the splitting takes place downwards, there is a risk of spreading infection to the compressor urethræ and so producing incontinence; if the splitting takes place upwards, the bladder neck is involved and the procedure is no longer extravesical. We have always maintained that it is easier to secure a watertight suture line in a conduit tube (the prostatic bed) than in a reservoir (the bladder), with its contracting and expanding wall; hence our advocacy of a purely extravesical technique. Any suturing in the region of the bladder neck, we feel, leads to a greater risk of stenosis at this danger-line. For this reason we do not favour the vesicocapsular procedure of Ogier Ward (1948).

To those who, like Couvelaire, advocate closure of the capsule in two or more layers, we would say that it is unnecessary, and the less catgut we insert into any potentially infected wound the better. With a carefully applied continuous suture, such as we advise, the incidence of suprapubic leakage is so low as to be insignificant. Couvelaire's own figures suggest a much higher incidence of postoperative leakage than ours.

The use of foreign bodies for hæmostasis in the prostatic cavity we do not favour. Some surgeons (Lowsley and Gentile 1948) use the bag of a Foley catheter in the cavity. This seldom exerts even pressure on the irregular bed, and is therefore of poor hæmostatic value; it causes painful spasms and prevents the rapid contraction of the cavity—nature's method of effecting hæmostasis. The use of absorbable packs—oxidised cellulose and alginates—have several additional disadvantages. If they disintegrate rapidly, fragments are apt to block the catheter and interfere with drainage: slow disintegration will lead to difficulty and even impossibility of micturition on withdrawing the catheter Should the latter have to be replaced, the reintroduction may be exceedingly difficult or impossible. Kovarovic (1947) has demonstrated radiologically that the lower ureters can be compressed by tight packing of the prostatic cavity.

Finally, we condemn wholeheartedly the technique of those who, professing to carry out a retropubic prostatectomy (their own modification, of course), in reality perform a "smash-and-grab" raid on the adenoma through a capsular incision, usually in a welter of blood, and effect a most perfunctory suture of the capsule, with interrupted sutures.

The operation, we submit, should be carried through step by step, under perfect vision, with gentleness, conforming to the accepted principles of modern surgical technique—namely, adequate exposure, careful hæmostasis, and accurate reposition of damaged parts. The retropubic operation, properly applied, allows for this.

CONCLUSIONS

The retropubic approach to the prostate conforms, we feel, most nearly to the modern surgical ideal.

We present our experience with the procedure in 757 cases, and reiterate our satisfaction. The results suggest that established prostatic obstruction should be relieved before renal impairment and advancing age add to the risk. Reasonably early intervention by the retropubic route offers a satisfactory functional result, with little risk and easy convalescence. The relief, moreover, should be permanent, for the whole of the existing obstructing tissue is removed.

As evidence that our happy experiences are not unique we take leave to quote from a recent article by Professor Cibert, of Lyons, whose retropubic experience now amounts to some 500 cases:

"Voici donc ce que m'a donné la prostatectomie de Millin. Malgré bien des imperfections encore (mais quelle méthode n'en a-t-elle pas?), mon impression d'ensemble est favorable: abaissement de la mortalité, extension de l'opérabilité à des malades considérés jusqu'à présent par moi comme hors d'atteinte, une simplicité habituelle des suites, une rapidité, hautement appréciées par les malades. Et la conviction étayée maintenant sur une expérience suffisante qu'aucune des méthodes que j'avais jusqu'à présent utilisées ne peut donner en série pareils résultats, du moins entre mes mains. C'est pourquoi je fais des rétropubiennes."

We wish to express our indebtedness to Mr. G. M. Lewis, F.R.C.S., Mr. H. N. G. Hudson, F.R.C.S., Mr. D. B. Duffy, F.R.C.S., Mr. R. P. M. Miles, F.R.C.S., and Dr. Lynn Evans, for their help in the laborious task of reviewing case-histories and in compilation of the statistics.

BIBLIOGRAPHY

Bacon, S. K. (1948) *J. Urol.* **59**, 376.
Bell, J. G. Yates (1947) *Lancet*, **ii**, 347.
Cibert, J. (1947) *Lyon chir.* **42**, 40.
— (1948) *J. Urol. méd. chir.* **54**, 207.
Couvelaire, R. (1947) *Ibid*, **53**, 352.
— (1948) L'adenectomie prostatique retropubienne, Paris.
de la Pena, E. (1947) *Med. esp.* **10**, 382.
Duvergey, H. (1947) *Gaz. Hôp., Paris*, **120**, 233.
Foret, E. (1947) *J. belge Urol.* **15**, 555.
Galbraith, W. W. (1948) *Proc. R. Soc. Med.* **41**, 73.
Gouverneur, R., Aboulker, P., Dufour, A. (1947) *J. Chir., Paris*, **63**, 425.
Hey, Wilson H. (1945) *Brit. J. Surg.* **33**, 41.
Kirz, E. (1947) *Ibid*, **34**, 272.
Kovarovic, K. (1947) *P. V. 41me. Congr. franç. Urol.*
Lowsley, O. S., Gentile, A. (1948) *J. Urol.* **59**, 281.
Millin, T. (1945) *Lancet*, **ii**, 693.
— (1946a) *Proc. R. Soc. Med.* **39**, 327.
— (1946b) *J. belge Urol.* **14**, 345.
— (1947) Retropubic Urinary Surgery, Edinburgh.
— (1948) *J. Urol.* **59**, 267.
Perrier, C. (1947) *Rev. méd. Suisse rom.* **67**, 300.
Savino, F. M. (1948) *Arch. esp. Urol.* **4**, 333.
van Gulik, F. H. (1946) *Ned. Tijdschr. Geneesk.* **90**, 1384.
Viollet, P. (1947) *Gaz. méd. limousine*, **40**, 195.
Walters, G. A. B. (1948) *Lancet*, **ii**, 638.
Ward, R. O. (1948) *Ibid*, **i**, 472.

GROWTH OF THE PRESCHOOL CHILD IN LONDON

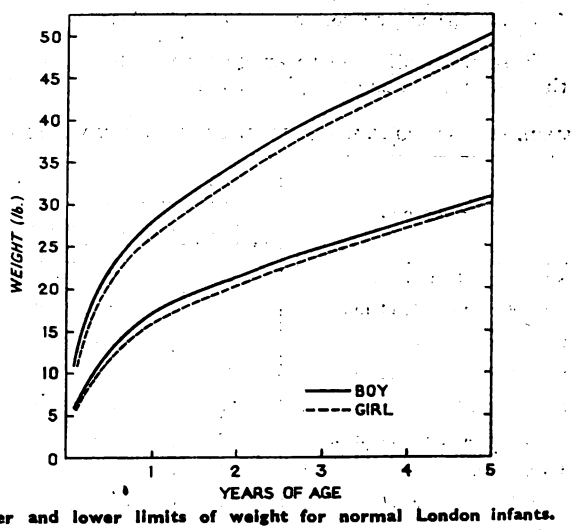
A. T. GORE, D.P.A. W. T. PALMER

From the Statistical Section, L.C.C. Public-health Department

MEDICAL workers responsible for nursery infants have been handicapped by the absence of any authoritative standard of weight against which to assess nutrition. Commonly, reference has been made to the American standard of Mitchell-Nelson[1] which is of doubtful application to English infants, and a desire has been expressed for a standard which could be confidently accepted as related to infants in this country.

To satisfy this demand to a limited extent (until a wider review can be organised) a pilot study of a sample of 5684 London infants has been made. By the courtesy

1. Nelson, W. E. Textbook of Pediatrics. Philadelphia, 1946.



Upper and lower limits of weight for normal London infants.

Digitized by Google

TABLE I—ACTUAL MEAN WEIGHTS AND STANDARD DEVIATIONS (WITH STANDARD ERRORS) OF LONDON INFANTS IN 1947

Age-group	Boys			Girls		
	No. measured	Mean weight (lb.)	Standard deviation (lb.)	No. measured	Mean weight (lb.)	Standard deviation (lb.)
2–5 weeks	141	8·8 ± 0·12	1·38 ± 0·08	136	8·7 ± 0·14	1·61 ± 0·10
6–9 ,,	148	11·1 ± 0·15	1·78 ± 0·11	136	10·4 ± 0·12	1·44 ± 0·08
10–13 ,,	120	13·1 ± 0·17	1·84 ± 0·12	139	12·1 ± 0·14	1·71 ± 0·10
4 months	116	14·6 ± 0·21	2·26 ± 0·15	130	13·7 ± 0·15	1·70 ± 0·11
5 ,,	140	16·1 ± 0·20	2·34 ± 0·14	95	15·3 ± 0·21	2·02 ± 0·15
6 ,,	124	17·6 ± 0·18	1·97 ± 0·13	124	16·5 ± 0·22	2·41 ± 0·16
7 ,,	106	18·6 ± 0·27	2·75 ± 0·19	111	17·3 ± 0·20	2·09 ± 0·14
8 ,,	118	19·7 ± 0·24	2·57 ± 0·17	88	18·5 ± 0·26	2·42 ± 0·18
9 ,,	97	20·4 ± 0·25	2·49 ± 0·18	105	19·1 ± 0·28	2·85 ± 0·20
10 ,,	84	21·1 ± 0·24	2·16 ± 0·17	81	20·2 ± 0·24	2·18 ± 0·17
11 ,,	68	22·4 ± 0·31	2·52 ± 0·22	73	20·7 ± 0·29	2·46 ± 0·21
1 yr.–1 yr. 2 mos.	251	23·0 ± 0·18	2·85 ± 0·13	226	21·4 ± 0·19	2·82 ± 0·13
1 yr. 3 mos.–1 yr. 5 mos.	172	24·6 ± 0·22	2·91 ± 0·16	148	22·8 ± 0·22	2·62 ± 0·13
1 yr. 6 mos.–1 yr. 8 mos.	127	26·2 ± 0·26	2·98 ± 0·18	147	24·2 ± 0·26	3·17 ± 0·18
1 yr. 9 mos.–1 yr. 11 mos.	97	27·4 ± 0·33	3·27 ± 0·23	122	26·9 ± 0·33	3·63 ± 0·23
2 yr.–2 yr. 2 mos.	93	28·8 ± 0·39	3·74 ± 0·28	96	27·4 ± 0·37	3·59 ± 0·26
2 yr. 3 mos.–2 yr. 5 mos.	106	29·4 ± 0·30	3·05 ± 0·21	100	28·7 ± 0·34	3·40 ± 0·24
2 yr. 6 mos.–2 yr. 8 mos.	83	31·7 ± 0·38	3·46 ± 0·27	80	29·3 ± 0·34	3·08 ± 0·24
2 yr. 9 mos.–2 yr. 11 mos.	82	32·1 ± 0·45	4·10 ± 0·32	89	30·8 ± 0·37	3·52 ± 0·26
3 yr.–3 yr. 5 mos.	172	33·8 ± 0·31	4·13 ± 0·22	133	32·5 ± 0·33	3·82 ± 0·23
3 yr. 6 mos.–3 yr. 11 mos.	192	35·2 ± 0·29	4·07 ± 0·21	199	34·6 ± 0·30	4·25 ± 0·21
4 yr.–4 yr. 5 mos.	177	37·2 ± 0·37	4·92 ± 0·26	169	36·3 ± 0·35	4·52 ± 0·25
4 yr. 6 mos.–4 yr. 11 mos.	67	38·5 ± 0·54	4·43 ± 0·38	76	37·6 ± 0·50	4·40 ± 0·35

of the medical officers of health concerned, details of the most recent measurements were copied from the infants' record cards at four London infant-welfare centres, one in each of the metropolitan boroughs of Fulham, Lewisham, St. Marylebone, and Shoreditch. The numbers of children whose measurements were noted were as follows:

	Boys	*Girls*	*Total*
Fulham	1034	1036	2070
Lewisham	958	898	1856
St. Marylebone	393	404	797
Shoreditch	496	465	961
Total	2881	2803	5684

The basic information was then transcribed to punched cards and the tabulations performed mechanically.

The various social indices for these four boroughs are as follows:

	Social index (a)	*Persons per dwelling (b)*	*Infant mortality 1931–40 (c)*
Fulham	28·7	5·57	56
Lewisham	22·7	4·58	46
St. Marylebone	27·8	4·81	66
Shoreditch	44·6	6·91	66
London A.C.	33·7	5·64	56

(*a*) Percentage of males aged 14 and over whose occupations were assigned to social classes IV and V at the 1931 census.
(*b*) 1931 census.
(*c*) Deaths under 1 year per 1000 live births.

It seems justifiable to suggest that the weighting of the boroughs in the sample is such as to give an approximation to average conditions for London as a whole. Though it is necessary to give this assurance, it was found (see below) that there were no statistically significant differences between borough average measurements.

ANALYSES

Owing to the size of the sample it was obvious from the outset that an individual age-group within a borough might be very small, and therefore the extra work involved in tabulating was undertaken so that dispersions could be calculated. This was done for each age-group within each borough, and mean weights with their standard errors were thus obtained for monthly intervals of age. These averages were then examined to determine (1) the smallest intervals of age required, and (2) whether the averages differed from borough to borough.

(1) The intervals of age selected were months up to 1 year; three months from 1 year to 3 years; and six months from 3 years to 5 years. There was no point in taking smaller intervals, since the dispersions were such that differences between successive smaller age-groups would not have been significant.

(2) Earlier investigations[2] having shown differences in average weights of school-children between London boroughs, it was suspected that there might be differences in the infants' weights. Up to about 18 months of age the differences in the means were neither statistically

2. L.C.C. Report of the School Medical Officer on the Average Heights and Weights of Elementary Schoolchildren in the County of London in 1938. London, 1940. Daley, W. A. *Med. Offr*, 1944, 71, 173; *Ibid*, 1948, 79, 242.

TABLE III—ACTUAL MEAN HEIGHTS AND STANDARD DEVIATIONS (WITH STANDARD ERRORS) OF LONDON INFANTS IN 1947

Age-group	Boys			Girls		
	No. measured	Mean height (in.)	Standard deviation (in.)	No. measured	Mean height (in.)	Standard deviation (in.)
1 yr.–1 yr. 5 mos.	27	30·7 ± 0·31	1·60 ± 0·22	32	29·7 ± 0·27	1·51 ± 0·19
1 yr. 6 mos.–1 yr. 11 mos.	37	32·6 ± 0·22	1·35 ± 0·16	41	31·6 ± 0·29	1·87 ± 0·21
2 yr.–2 yr. 5 mos.	64	34·1 ± 0·24	1·96 ± 0·17	63	33·8 ± 0·26	2·07 ± 0·18
2 yr. 6 mos.–2 yr. 11 mos.	63	35·8 ± 0·21	1·65 ± 0·15	68	35·2 ± 0·22	1·83 ± 0·16
3 yr.–3 yr. 5 mos.	79	37·6 ± 0·29	2·57 ± 0·20	58	36·8 ± 0·28	2·15 ± 0·20
3 yr. 6 mos.–3 yr. 11 mos.	82	38·9 ± 0·25	2·30 ± 0·18	87	38·7 ± 0·18	1·71 ± 0·13
4 yr.–4 yr. 5 mos.	80	39·9 ± 0·23	2·03 ± 0·16	70	39·3 ± 0·36	2·97 ± 0·25
4 yr. 6 mos.–4 yr. 11 mos.	36	40·9 ± 0·31	1·89 ± 0·22	34	40·6 ± 0·35	2·06 ± 0·25

Digitized by Google

significant nor consistent. From 18 months onwards there were consistent differences, but, owing to the smallness of the sample, none reached a statistically significant level.

The figures for the four boroughs were therefore pooled and the result accepted as typical of the whole county. Table I gives the mean weights and standard deviations, each with its standard error, for the pooled observations, in the selected age-groups, for boys and girls separately.

Graduation.—To assist the interpolation necessary for setting up a standard weight scale at equal age intervals, the data of table I were graduated algebraically. The final graduated standard, set out in table II, gives mean weights and standard deviations for both boys and girls at weekly intervals up to 3 months, monthly intervals up to 1 year, and quarterly intervals up to 5 years. This survey therefore links up with the previous surveys of school-children [2] thus providing standards for London children from birth to school-leaving age.

Infants' Weight Charts.—The disadvantage of using "average weight for age" as an index of general health is the very wide dispersion that normally occurs. The standard deviations set out in table II can be used to mitigate this difficulty by establishing upper and lower margins outside which it is improbable that a normal child's weight would lie. By taking the margins given by the mean weight plus or minus twice the standard deviation we obtain limits within which will fall the weights of 95% of normal children. This is illustrated in the accompanying diagram and it is suggested that, if a standard is to be printed on a weight chart, this form of margin indication is far more useful than the normal single curve giving the "average weight." In practice more than one chart will be used to cover the range from birth to entry to school, but table II gives all the information likely to be required for plotting any desired "limit curves."

Stature.—It is regretted that only 921 (16%) of the infants surveyed had their heights recorded, and all of these were aged over 1 year. Such a sample is far too small, but in view of the need for any information, however scanty, it was decided to take out the averages for what they were worth. Table III gives these mean heights and standard deviations, for boys and girls, at six-monthly intervals from 1 to 5 years of age.

Since this sample was not only small but also could not be regarded as representative (70% of the infants whose heights were recorded were from one borough), no attempt was made to graduate the data or to calculate a set of standard heights. For the same reasons no attempt was made to investigate whether any weight-for-height index was indicated by the data.

TABLE II—GRADUATED MEAN WEIGHTS AND STANDARD DEVIATIONS OF LONDON INFANTS IN 1947

Central age	Boys		Girls	
	Mean weight (lb.)	Standard deviation (lb.)	Mean weight (lb.)	Standard deviation (lb.)
4 weeks	8·60	1·38	8·53	1·37
5 ,,	9·17	1·46	8·96	1·43
6 ,,	9·71	1·54	9·39	1·48
7 ,,	10·24	1·61	9·80	1·54
8 ,,	10·75	1·67	10·21	1·59
9 ,,	11·24	1·74	10·62	1·64
10 ,,	11·71	1·80	11·01	1·69
11 ,,	12·18	1·85	11·40	1·74
12 ,,	12·62	1·91	11·78	1·78
13 ,,	13·05	1·96	12·16	1·82
4 months	14·74	2·14	13·69	1·99
5 ,,	16·20	2·27	15·09	2·11
6 ,,	17·46	2·36	16·36	2·21
7 ,,	18·56	2·45	17·49	2·31
8 ,,	19·55	2·52	18·49	2·39
9 ,,	20·47	2·58	19·34	2·44
10 ,,	21·22	2·61	19·97	2·46
11 ,,	21·95	2·63	20·53	2·48
12 ,,	22·59	2·71	21·03	2·52
1 yr. 3 mos.	24·08	2·89	22·55	2·71
1 yr. 6 mos.	25·53	3·06	24·05	2·89
1 yr. 9 mos.	26·95	3·23	25·52	3·06
2 yr.	28·31	3·40	26·92	3·23
2 yr. 3 mos.	29·59	3·55	28·24	3·39
2 yr. 6 mos.	30·78	3·69	29·46	3·54
2 yr. 9 mos.	31·88	3·83	30·57	3·67
3 yr.	32·81	3·94	31·55	3·79
3 yr. 3 mos.	33·69	4·04	32·58	3·91
3 yr. 6 mos.	34·66	4·16	33·59	4·03
3 yr. 9 mos.	35·65	4·28	34·59	4·15
4 yr.	36·64	4·40	35·58	4·27
4 yr. 3 mos.	37·62	4·51	36·58	4·39
4 yr. 6 mos.	38·61	4·63	37·58	4·51
4 yr. 9 mos.	39·60	4·75	38·57	4·63
5 yr.	40·59	4·87	39·57	4·75

We are grateful to Sir Allen Daley, the county M.O.H., for permission to publish this paper; Mr. B. Benjamin, the statistician, for advice and criticism; and the medical officers of health of the four boroughs for access to their records. The L.C.C. takes no responsibility for the opinions expressed, which are personal only.

PAROXYSMAL COLD HÆMOGLOBINURIA OF NON-SYPHILITIC TYPE

L. K. MALLEY
M.D. N.U.I.
PHYSICIAN TO OUTPATIENTS

M. D. HICKEY
M.D., M.Sc. N.U.I., F.R.C.P.I., D.P.H.
PATHOLOGIST

MATER MISERICORDIÆ HOSPITAL, DUBLIN

PAROXYSMAL cold hæmoglobinuria has become established as a clinical entity and is the best-known of the essential hæmoglobinurias. Dressler (1854) has been credited with the report of the first case, and since then about 350 cases have been published.

A typical paroxysm is preceded by certain prodromal symptoms, is produced by a lowering of the surface temperature of the body, and in most instances is attended by a constitutional reaction associated with hæmoglobinæmia and hæmoglobinuria. The attack is usually of short duration, and vasomotor disturbances of the Raynaud type are often present. It is often accompanied by a reduction in the number of red blood-cells and in the percentage of hæmoglobin, which are usually within normal limits between attacks. A typical attack may be induced by immersing the upper and lower extremities in ice-cold water for 10–20 min. (Rosenbach 1880).

In the great majority of cases there is either clinical or serological evidence of congenital or of acquired syphilis, and the unique hæmolysin first demonstrated by Donath and Landsteiner (1904) is found. Effective antisyphilitic therapy leads to a cessation of the attacks of hæmoglobinuria, disappearance of the hæmolysin, and a reversal of the serological tests for syphilis. These findings clearly distinguish this type from all other forms of paroxysmal hæmoglobinuria. Extensive reviews of this disorder have been published by Mackenzie (1929) in the United States, and Cattaneo (1931) in Italy.

In recent years attention has been drawn to a separate form of paroxysmal hæmoglobinuria induced by exposure of the body to cold in which clinical and serological evidence of syphilis is absent and the Donath-Landsteiner reaction is negative. A feature of these cases is the presence of a cold agglutinin in high titre. Stats and Wasserman (1943), who first clearly distinguished between the two types of paroxysmal cold hæmoglobinuria, collected 10 published cases (Mino 1924, Alexander and Thompson 1925, Stieffel 1928, Roth 1935, Salén 1935, Kopplin 1936 (2 cases), McCombs and McElroy 1937, Hanns and Sommer 1938, Stats and Bullowa 1943). Stats and Wasserman produced experimental evidence, which was subsequently elaborated in more detail by Stats (1945), suggesting that the hæmolysis in the non-syphilitic type was due to an increased susceptibility of the patient's erythrocytes

Digitized by Google

to mechanical trauma and differed fundamentally from the hæmolysis produced by the Donath-Landsteiner hæmolysin.

In view of the apparent rarity of this form of paroxysmal cold hæmoglobinuria we report here in some detail a case which we have studied over the past four years.

A retired schoolmaster, aged 69, was admitted to hospital on March 16, 1944. The family history was irrelevant. The patient was a married man with nine children, all of them alive and well. In 1929 he had had a perforating injury of the right eye followed by keratitis; otherwise he had had no serious illness. There was no history of venereal disease or of malaria.

Early in January, 1944, the patient noted for the first time a dusky blue discoloration of the fingers, lobes of the ears, and tip of the nose on exposure to cold. These attacks occurred frequently and often terminated spontaneously. They could be cut short by entering a warm room. On Jan. 29 he voided dark red urine. Before admission he had three attacks in which he passed dark urine. These occurred in the afternoon on very cold days. The discoloration was present only in one or two voidings of urine and was associated with colour changes in the hands. The patient had slight dyspnœa on exertion and his sleep was disturbed by frequency of micturition.

On Admission.—He was tall and thin, with grey hair. His skin and visible mucosæ were very pale, with a lemon-yellow tint most pronounced in the face and scleræ. He was blind in the right eye, owing to a corneal scar, and edentulous. Pulse regular, rate 75 per min. Blood-pressure 140/80 mm. Hg. Pulmonary emphysema and chronic bronchitis were present. The liver and spleen were not palpable. Neurological examination showed no abnormality. The prostate gland was slightly enlarged. Pulsation of the arteries in the upper and lower limbs was normal. Electrocardiograms were normal.

Raynaud Phenomenon.—Paroxysmal colour changes in the fingers, nose, and ears were frequently observed, most often in the morning, but on very cold days throughout the day. These changes affected the fingers of both hands, which became cold to touch and bluish-black. The execution of fine movements became difficult, and the patient had "pins-and-needles" in them. At the same time the lobes of the ears and the tip of the nose turned dusky. The feet did not change colour but became appreciably cooler. The attacks lasted from several minutes to two hours, depending mainly on the degree of exposure to cold, the temperature of the room, and the efforts made by the patient to warm his hands. An attack was readily produced if the patient kept his hands outside the bed-clothes on waking in the morning. As an attack came to an end, the fingers, ears, and nose turned beefy red before resuming their normal appearance. The radial pulses were easily felt during the attacks, and there was no alteration in the blood-pressure. Local syncope was not noted, and there was little or no pain. The nail beds did not show trophic changes or gangrene.

Hæmoglobinuria.—Three attacks of hæmoglobinuria came on while the patient was in hospital. One attack was spontaneous and took place on a very cold day. The other attacks were induced by the Rosenbach test. In the spontaneous attack the discoloration of the urine appeared in the afternoon and was present in two voidings of urine. Apart from a feeling of intense cold in the feet there were no prodromal symptoms —e.g., aching and pain in the back, legs, or abdomen; cramps; headaches; or intestinal disturbance—nor did the patient complain of a chill or have a raised temperature, increased pulse-rate, or altered blood-pressure.

Investigation of Urine.—During the four years the patient was under observation his urine was repeatedly examined, both during the paroxysms of hæmoglobinuria and in the long intervals between the attacks. During a paroxysm the urine was of the colour of burgundy, of high specific gravity (sp. gr. 1·024–1·026), and contained a considerable amount of albumin, no sugar, and some urobilinogen. The benzidine test was positive, and spectroscopy showed the bands of oxy-hæmoglobin. The centrifuged sediment contained granular and epithelial casts but no red blood-cells. In the intervals between attacks the benzidine test was negative, hæmosiderin was absent (prussian-blue reaction), and spectroscopy did not show oxyhæmoglobin. In the early stages of the investigation a faint trace of albumin was found, but later a moderate albuminuria was constant.

Investigation of Blood

At first counting the red blood-cells was difficult because of auto-agglutination in the pipette, but this was later overcome by diluting the blood in Hayem's solution warmed to 37°C. Hæmagglutination, however, prevented the preparation of satisfactory films from the bone-marrow. Over the four years of observation the erythrocytes varied from 2,910,000 to 3,720,000 per c.mm., Hb from 55 to 85% (16 g.=100%), colour-index from 1·00 to 1·25, leucocytes from 6600 to 10,050 per c.mm., and blood-platelets from 200,000 to 500,000 per c.mm. A typical differential count was neutrophils 61%, basophils 1%, eosinophils 1%, lymphocytes 22%, and mononuclear cells 15%. The reticulocyte-count was usually about 12% after an attack, and consistently raised between attacks (2–8%).

A Price-Jones curve (constructed on Nov. 7, 1945, when the red-cell count was 3,030,000 per c.mm., Hb 61%, M.C.V. 105·6 c.μ, and M.C.H.C. 30%) showed a mean cell diameter of 8·56 μ, standard deviation 0·8904, and coefficient of variation 10·16%; van den Bergh reaction indirect; the serum-bilirubin varied from 3·6 to 5·78 mg. per 100 ml. Methæm-albumin was demonstrated in the serum by a positive Schumm test (Fairley 1941). Blood group $BMRh_1$. Erythrocyte-sedimentation rate 107 mm. in one hour at 15°C (Westergren).

Liver-function tests gave normal results. Blood Wassermann and Kahn tests were negative. The cerebrospinal fluid was normal. Donath-Landsteiner phenomenon not present; the test was repeated on numerous occasions both during and in the intervals between the attacks of hæmoglobinuria. Guineapig complement was added. The duration of exposure to cold was varied from 5 to 30 min. Duplicate tests performed in an atmosphere of 10% CO_2 (Wagley et al. 1947) all gave negative results. The acid hæmolysis test (Ham 1939) was negative. Coombs's test (Coombs et al. 1945) was positive. The patient's erythrocytes after being thoroughly washed in physiological saline solution at 37°C were agglutinated by an anti-human-globulin serum. The test was positive at 16°C and 37°C. The positive result at 37°C excluded the possibility of the results being due to some of the cold agglutinin remaining attached to the red blood-cells in spite of the thorough washing at 37°C.

An auto-agglutinin of high titre, active at room temperature and more strongly active in the cold, was constantly present in the patient's serum. This agglutinin possessed the characteristics of a typical cold agglutinin as defined by Stats and Wasserman (1943). It showed thermal amplitude 0–30°C; reversibility; a similar titre when tested against the patient's erythrocytes and against erythrocytes of a compatible ABO group; and thermostability, being stable for a long time when stored in a refrigerator, and not inactivated by heating to 56°C for 15 min. The titre of the cold agglutinin remained constant throughout the period of observation at a mean titre of 1/2048. The final cell suspension used in the test was 1%. The results were read macroscopically when the tubes had stood for two hours in the refrigerator in a water-bath containing melting ice. Titrations both during and after the paroxysms of hæmoglobinuria showed that the titre was unaffected by the attacks.

The osmotic fragility of the red cells (Creed 1938) was normal. Hæmolysis began at 0·28% and was complete at 0·44% sodium chloride. The mechanical fragility (Shen et al. 1944) was as follows:

Temperature	*Oxalated whole blood, hæmatocrit 30%*		*Washed* erythrocytes, 30% suspension*	
	Patient	*Normal control*	*Patient*	*Normal control*
	Hæmolysis		*Hæmolysis*	
16°C	77%	2·6%	8·6%	5·5%
27°C	54%	2·0%		
37°C	6·8%	0·34%		

* Cells washed in physiological saline at 37°C.

The hæmatocrit of the control blood was adjusted to 30% by addition of its own plasma; 0·5 ml. of each blood or cell suspension was used as a blank, and a further 0·5 ml. completely hæmolysed to give the reference value of 100% hæmolysis. In the experiment 0·5 ml. of each specimen was placed in a 50 ml. rubber-stoppered conical flask containing ten glass beads 4 mm. in diameter. The flasks were held horizontally, clipped to the periphery of a wheel 22 cm. in diameter rotated for an hour at 40 r.p.m. The hæmolysis resulting in each specimen was determined by the Klett-Summerson photo-electric colorimeter.

Digitized by Google

Immersion of Extremities in Cold Water (Rosenbach test)

Test 1: the patient's hands were immersed in cold water containing melting ice for 15 min. Raynaud's phenomenon appeared an hour later. Urine passed two and five hours after the test was dark and contained hæmoglobin. A specimen passed twelve hours after the test was free from hæmoglobin.

Test 2: A specimen of blood was collected from the right arm before immersion was begun. Hæmoglobin was not present in the serum (absorption bands of hæmoglobin were not visible in a 2 cm. depth of serum). A sample of urine contained no hæmoglobin. The left hand and the left foot were immersed in water at 12°C. After 15 min. patchy areas of cyanosis appeared on the fingers of the right hand. Hæmoglobin was not present in the serum of blood now collected from the right arm. After a further 15 min. the right foot was also immersed, and the temperature of the water reduced to 8·5°C. A tourniquet was applied 5 min. later to the left arm above the elbow, and the patient was instructed to exercise the fingers of the hand vigorously. After 5 min. exercise blood was collected from the left arm, and the tourniquet was removed. The serum contained hæmoglobin 460 mg. per 100 ml. The exposure to cold was terminated 5 min. later—i.e., 45 min. from the start of the experiment. Samples of urine collected at intervals from the termination of immersion gave the following findings:

Time from end of test	*Colour*	*Benzidine test*
15 min.	Yellow	Positive, absorption bands of oxyhæmoglobin present
4 hours	Burgundy	Strongly positive
6 hours	Amber	Strongly positive
8 hours	Yellow	Faintly positive
10 hours	Yellow	Faintly positive
20 hours	Yellow	Negative

The positive effects of exercise and of the tourniquet were next investigated by tests 3 and 4.

Test 3: Blood was taken from the left arm. Hæmoglobin not present in the serum. The cuff of a sphygmomanometer was next placed on the right arm to exert a pressure of 40–50 mm. Hg, and the arm was immersed in water at 8°C for 10 min., no movement of the fingers being allowed. At the end of 10 min. the pressure in the cuff was raised to 125 mm. Hg, and the arm was gently lifted out of the water-bath. Blood was taken from the right arm. The serum contained hæmoglobin 298 mg. per 100 ml. An hour later blood was taken from the right arm. Hæmoglobin was not present in the serum.

Test 4: Test 3 was repeated without application of a sphygmomanometer cuff. The results were similar. At the end of 10 min. of exposure to cold the serum of a blood sample taken from the chilled arm contained hæmoglobin 373 mg. per 100 ml. Blood was also collected from the other arm at the same time. The serum of this specimen did not contain hæmoglobin. Urine passed 4 and $7^1/_2$ hours after exposure to cold did not contain hæmoglobin.

The osmotic fragility of the red blood-cells before and after 15 min. of chilling, and $3^1/_2$ hours from the end of chilling in test 2 was unchanged.

Application of Ice to Skin.—Application of a cube of ice to the skin of the forearm for 10 min. produced no change in colour, weal, or flare, and no urticarial response could be demonstrated.

Progress of Patient

The patient attended regularly at the outpatient department from April 11, 1944, to Feb. 23, 1948.

During the summer of 1944 no attacks occurred. After the patient had left hospital, hæmoglobinuria was first noted on Nov. 3, 1944. From that date until May 5, 1945, hæmoglobinuria occurred on nineteen days. It was again absent in the summer of 1945 and recurred on Oct. 20, 1945, from which date until March 3, 1946, it was present on six days. The summer of 1946 was also free from hæmoglobinuria. From Dec. 17, 1946, to April 9, 1947, attacks occurred on five days. Most of these attacks took place on exceptionally cold days.

From the winter of 1945 the patient took the precaution of wearing extra heavy clothing on the body, thick gloves, and two pairs of heavy stockings, and he avoided going out of doors on very cold days. Nearly all subsequent attacks took place when circumstances compelled him to go out on a cold day. There was no attack of hæmoglobinuria after April 9, 1947, and we attribute this to the precautions which he took.

The patient was admitted to hospital on Feb. 23, 1948, for a routine check-up. General physical findings had not changed since the date of the initial examination. The blood Wassermann, Kahn, and Donath-Landsteiner tests were negative. The titre of the cold agglutinin was 1/4096.

Readmission

The patient was readmitted to hospital on Aug. 15, 1948, with acute urinary obstruction due to prostatic enlargement. A blood-count showed red cells 1,730,000 per c.mm., Hb 5·6 g. per 100 ml., white cells 11,700 per c.mm. (neutrophils 82%, lymphocytes 15%, monocytes 3%). Blood-urea 60 mg. per 100 ml. Urine heavily infected with coliform organisms. His clinical condition precluded surgical intervention, and his bladder was drained through an indwelling catheter. There was no response to treatment, and he died on Sept. 2, 1948, aged 72.

Post-mortem Findings

Necropsy five hours after death showed the body of a rather poorly nourished elderly male with a healed scar on the right cornea. There was no jaundice.

The *brain* weighed 1350 g. and appeared normal.

The *heart* weighed 350 g. with the roots of the great vessels attached. The pericardial cavity contained 20 ml. of straw-coloured fluid. There were no valvular abnormalities or pericarditis. There was minimal atheroma of the coronary arteries, with no diminution of their lumina.

Lungs.—The right lung weighed 705 g. and bore old scars at the apex. The lower lobe was congested and œdematous, and there were slight congestion and œdema of the upper and middle lobes. The left lung weighed 603 g. and had adhesions at the apex. Congestion and œdema were well-marked in the lower lobe, and slight in the upper lobe. Microscopically there was generalised œdema. Fibrin thrombi, some of which showed hyaline change, were found in a few of the smaller vessels. Scattered throughout these thrombi were numerous phagocytes containing a bright yellow pigment, probably hæmatoidin. A few of these phagocytes gave a diffuse prussian-blue reaction for iron. Phagocytes containing iron-free pigment were numerous in the walls of the alveoli.

The *peritoneum* was normal and there was no thrombosis of portal, splenic, or mesenteric vessels.

The *liver* weighed 1632 g. The surface was smooth. The organ as a whole was red-brown but was deeply bile-stained at the lower borders. It gave a strong prussian-blue reaction for iron. There was no macroscopic evidence of venous thrombosis. The gall-bladder was thin-walled and contained no calculi. Microscopically the architecture of the liver was normal. The nuclei of the liver cells stained evenly and appeared normal. The cytoplasm of almost all the liver cells contained a considerable quantity of fine granular pigment, which gave the prussian-blue reaction for iron. At the periphery of the lobules the liver cells also contained a little yellow granular pigment, which did not give the reaction for iron. Since there was no bile retention in the biliary capillaries or in the small bile-ducts, this pigment was probably hæmatoidin. There was no increase in fibrous tissue between the lobules. Thrombi consisting of fibrin, red cells, and large phagocytes were found in many of the branches of the portal vein. The phagocytes contained much iron pigment.

The *stomach* was dilated and thin-walled, and its fundal mucosa showed no rugæ. The *intestines*, *pancreas*, and *suprarenal glands* were normal.

Kidneys.—The right kidney weighed 142 g., and the left 187 g. The surface of both was granular. Macroscopically the prussian-blue reaction was strongly positive both in the cortex and, slightly less intensely, in the pyramids. Several abscesses, the largest measuring 1·5 cm. in diameter, were scattered throughout both kidneys. The lower third of the right kidney was black. The right ureter was gangrenous. The histological picture was complicated by the presence of a severe pyelonephritis with abscess formation. Sections were cut of areas free from abscesses. In these areas the glomeruli were normal. There was severe albuminous degeneration of the epithelial cells lining the convoluted tubules. Pigment granules were numerous in the epithelium of the loops of Henle and in the collecting tubules. Most of this pigment gave a strong prussian-blue reaction. The interstitial tissue was increased in amount and showed hyaline change. No thrombi were seen.

Urinary Bladder.—The wall was thickened and small diverticula were present.

The *prostate gland* weighed 70 g. and measured 5·5 × 5 × 4 cm. Microscopically a benign hyperplasia was found.

Digitized by Google

The *spleen* weighed 240 g. and measured 13 × 9 × 4·5 cm. It showed no infarction, no splenculi, and no perisplenitis, was firm in consistence, and its cut surface was homogenous. Microscopically the spleen was extremely avascular. The cellularity of the pulp was greatly reduced by the presence of an excess of hyaline interstitial material. In most areas this hyaline material was homogenous, structureless, and eosinophilic. In others it was composed of numerous circular bodies 4–8 μ in diameter. These were apparently agglutinated and hæmolysed red blood-cells in the process of conversion into hyaline material. The malpighian corpuscles were not prominent. Many of the sinuses contained organised thrombi. Scattered diffusely throughout the pulp were many coarse pigment granules. Some of these gave the reaction for iron, but most did not. Pigment was also abundant in the fibrous tissue of the trabeculæ in the form of fine yellow granules, which did not give the reaction for iron.

The *lymphatic glands* were normal.

In the *venous system* no macroscopic thromboses were found.

Bone-marrow.—Red marrow extended two-thirds of the way down the shaft of the femur. The marrow of the ribs, sternum, and vertebral bodies was dark red. Microscopically the sternal marrow was highly cellular and contained little adipose tissue. Erythroblastic elements were much in excess of leucoblastic. A few megakaryocytes were seen. Erythropoiesis was of the normoblastic type.

DISCUSSION

The case-record here presented supports the opinion expressed by Stats and Wasserman (1943) and others of the existence of a hitherto unrecognised form of paroxysmal cold hæmoglobinuria not related to syphilis, and confirms their observations that the red blood-cells of patients with this form of hæmoglobinuria show an increased susceptibility to mechanical trauma. In the present case agglutination of the red cells by the cold agglutinin was probably largely responsible for this increased fragility. However, when the test was carried out on whole blood at a temperature at which agglutination did not take place—i.e., 37°C—or when washed red cells were used, the fragility, though considerably reduced, was still abnormal. We are uncertain about the influence of these findings on the hæmolytic episodes observed in this patient. It is to be noted that hæmolysis was produced by chilling of the patient's upper extremity without exercise. In our opinion the precise mechanism by which hæmolysis is produced in this syndrome is not yet established.

Death was due to urinary obstruction and ascending urinary infection following prostatic enlargement. Frequent urine examinations during four years up to June, 1948, showed that this infection was of recent origin. There was no hydronephrosis. The pyelonephritis was acute, with minimal fibrous-tissue reaction round the abscesses. Therefore the infection may reasonably be regarded as a terminal event which has no bearing on the main features of the case.

The remaining pathological findings are those of a hæmolytic anæmia in which intravascular hæmolysis has taken place. The numerous microscopic thrombi probably resulted from the presence of erythrocyte stromata in the circulation. Thrombi of a similar nature were described by Scott et al. (1938) in two cases of the Marchiafava-Micheli syndrome and were regarded by them as the result of emboli formed by erythrocyte stromata. The necropsy findings cannot be compared with those of previous cases, since necropsies are not included in any of the previous reports of this syndrome.

SUMMARY

A case is reported of paroxysmal cold hæmoglobinuria of the non-syphilitic type in a man, aged 69, who was observed over four years.

Clinical and serological evidence of syphilis was absent, and the Donath-Landsteiner reaction was negative.

Hæmatological investigation showed the presence of chronic hæmolytic anæmia.

A high-titre cold agglutinin was constantly present in the patient's serum.

Increased susceptibility of the patient's red cells to mechanical trauma was demonstrated.

The necropsy findings are described.

REFERENCES

Alexander, H. L., Thompson, L. D. (1925) *J. Amer. med. Ass.* **85**, 1707.
Cattaneo, L. (1931) *G. ital. Derm. Sif.* **72**, 1159.
Coombs, R. R. A., Mourant, A. E., Race, R. R. (1945) *Brit. J. exp. Path.* **26**, 255.
Creed, E. F. (1938) *J. Path. Bact.* **46**, 331.
Donath, J., Landsteiner, K. (1904) *Münch. med. Wschr.* **51**, 1590.
Dressler (1854) *Arch. path. Anat.* **6**, 264.
Fairley, N. H. (1941) *Quart. J. Med.* **10**, 95.
Ham, T. H. (1939) *Arch. intern. Med.* **64**, 1271.
Hanns, A., Sommer, A. (1938) *Strasbourg-méd.* **98**, 172.
Kopplin, F. (1936) *Z. klin. Med.* **130**, 784.
McCombs, R. P., McElroy, J. S. (1937) *Arch. intern. Med.* **59**, 107.
Mackenzie, G. M. (1929) *Medicine, Baltimore*, **8**, 159.
Mino, P. (1924) *Dtsch. med. Wschr.* **50**, 1533.
Rosenbach, O. (1880) *Berl. klin. Wschr.* **17**, 132.
Roth, G. (1935) *Proc. Mayo Clin.* **10**, 609.
Salén, E. B. (1935) *Acta med. scand.* **86**, 570.
Scott, R. B., Robb-Smith, A. H. T., Scowen, E. F. (1938) *Quart. J. Med.* **7**, 95.
Shen, S. C., Castle, W. B., Fleming, E. M. (1944) *Science*, **100**, 387.
Stats, D. (1945) *J. clin. Invest.* **24**, 33.
— Bullowa, J. G. M. (1943) *Arch. intern. Med.* **72**, 506.
— Wasserman, L. R. (1943) *Medicine, Baltimore*, **22**, 363.
Stieffel, R. (1928) Paris thesis, no. 72.
Wagley, P. F., Zinkham, W. H., Siebens, A. A. (1947) *Amer. J. Med.* **2**, 342.

SURVIVAL OF TRANSFUSED ERYTHROCYTES FROM A DONOR WITH NOCTURNAL HÆMOGLOBINURIA

J. V. DACIE, M.B. Lond., M.R.C.P.
P. L. MOLLISON, M.D. Camb., M.R.C.P.

From the Department of Clinical Pathology and the Medical Research Council Blood Transfusion Research Unit, Department of Obstetrics, Postgraduate Medical School of London

NOCTURNAL hæmoglobinuria, or the Marchiafava-Micheli disease, is an uncommon but characteristic type of chronic hæmolytic anæmia. The available evidence suggests that the hæmolysis is due to an abnormality of the patient's erythrocytes; and it has been shown that transfused normal erythrocytes survive for the normal period of 100–120 days in these patients (Mollison 1947, Dacie 1948). Though hæmolysis of such a patient's erythrocytes in autogenous and normal serum has been repeatedly demonstrated in vitro, the rate of elimination of the patient's cells in normal recipients does not seem to have been studied.

We present here details of the survival of erythrocytes taken from a patient with nocturnal hæmoglobinuria and transfused to two different recipients, one an adult and the other an infant. Elimination was more rapid than normal in both recipients, but the elimination was distinctly less rapid in the infant than in the adult. This difference, demonstrated in vivo, was paralleled by a difference in the hæmolytic activity of the two sera in vitro.

METHODS

Estimation of Survival-rate of Transfused Erythrocytes.—The blood donor, a man, aged 44, had typical nocturnal hæmoglobinuria. Details of his clinical history and laboratory findings have been reported elsewhere (Dacie 1948). His blood-group was O and he was Rh-positive. In August, 1947, when his erythrocyte-count was 1,800,000 per c.mm. and hæmoglobin level 8 g. per 100 ml., 420 ml. of blood was withdrawn into 120 ml. of acid sodium citrate — glucose diluent. An hour later the donated blood, which was unhæmolysed, was transfused to a group-B Rh-positive patient with rheumatoid arthritis and mild secondary anæmia. The survival of the transfused erythrocytes was studied by a modification (Dacie and Mollison 1943) of Ashby's (1919) differential agglutination method, using a potent anti-B serum.

In January, 1948, the donor was bled again, but this time only 170 ml. was taken into 50 ml. of the same

Digitized by Google

anticoagulant solution. On this occasion the donor had 1,400,000 red cells per c.mm. and 5 g. of hæmoglobin per 100 ml. This blood was stored at 4°C over night, and next morning some of the supernatant citrated plasma, which contained no obvious free hæmoglobin, was removed to give a slightly concentrated suspension of erythrocytes; 35 ml. of this suspension, together with 25 ml. of a slightly more concentrated suspension of erythrocytes from a normal group-A Rh-negative donor, was transfused to an anæmic premature infant (group A, Rh-positive). The rates of elimination of the two populations of donor erythrocytes were studied, using anti-A and anti-Rh sera of high titre and avidity.

Studies in Vitro.—The rates of hæmolysis of the donor's erythrocytes in the baby's serum and in the sera of normal adults were estimated in vitro.

The sera were obtained by defibrination of venous blood in an open flask. In the case of the baby the blood was withdrawn from the external jugular vein. Tests were carried out on the day of collection, the sera being kept frozen until used. The cells were obtained from the patient with nocturnal hæmoglobinuria already described and from another patient with nocturnal hæmoglobinuria and were well washed in isotonic saline.

To 0·5 ml. volumes of serum, 50 c.mm. volumes of *N*/10, *N*/5, *N*/4·5, and *N*/4 hydrochloric acid were added. Then 50 c.mm. volumes of a 50% suspension of washed erythrocytes from one of the patients with nocturnal hæmoglobinuria were added to each tube. The tubes were placed in a water-bath at 37°C and centrifuged after incubation for 30 min. This preliminary experiment showed which strength of acid was necessary to produce the greatest hæmolysis. Usually *N*/5 was required (see Dacie and Richardson 1943).

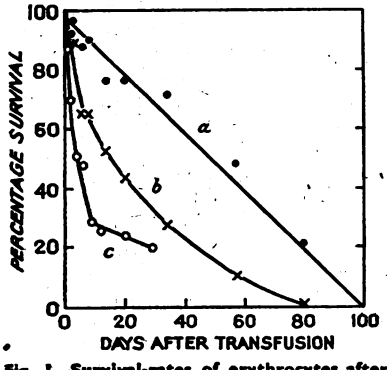


Fig. 1—Survival-rates of erythrocytes after transfusion: *a*, from normal adult donor to anæmic premature infant; *b*, from adult with nocturnal hæmoglobinuria to same infant; *c*, from same adult with nocturnal hæmoglobinuria to anæmic adult.

To 3·0 ml. of serum, to which had been added 0·3 ml. of the selected acid concentration, 0·3 ml. of the erythrocyte suspension was now added. Then 0·5 ml. was immediately withdrawn and centrifuged to obtain a control sample, and the remainder was placed in a water-bath at 37°C and incubated. At 5, 10, 20, and 30 min., 0·5 ml. samples were withdrawn, immediately chilled, and then centrifuged so that samples of the supernatant serum could be obtained as quickly as possible. Finally, equal volumes of the serum samples and of the remainder of the uncentrifuged cell-serum mixture were diluted in *N*/400 sodium hydroxide. Hæmoglobin liberated into the serum was then estimated as oxyhæmoglobin, a photo-electric colorimeter with a green filter being used.

RESULTS

Survival of Donor's Erythrocytes in Adult Recipient

The transfusion of the donor blood was completed in 1¾ hours. A sample taken 10 min. later contained only 174,000 donor cells per c.mm. This was about the number expected in view of the donor's low erythrocyte-count. Samples taken next morning and on subsequent occasions showed even lower concentrations of the donor's erythrocytes. Therefore the concentration found immediately after transfusion was taken as 100% survival, and subsequent counts were expressed as percentages of this figure. In fig. 1 the percentages have been plotted against time. It will be noted that elimination was rapid, 50% of the cells disappearing from the recipient's circulation in about 5 days, and by the 10th day only 30% were left. However, elimination

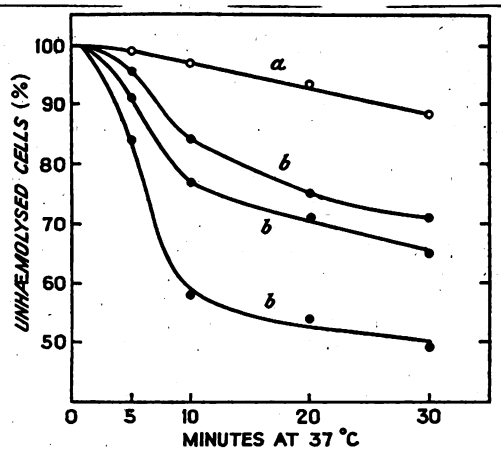


Fig. 2—Time-hæmolysis curve of erythrocytes from a patient with nocturnal hæmoglobinuria: *a*, in serum of anæmic premature baby; *b*, in sera of three normal adults.

of the remaining erythrocytes was slow, there being still about 20% surviving after a further 20 days.

Survival of Donor's Erythrocytes in Infant Recipient

The transfusion was completed in about 15 min., and a sample taken about half an hour later contained 822,000 group-O erythrocytes per c.mm.—i.e., erythrocytes from the patient with nocturnal hæmoglobinuria. Next day the concentration was 888,000 per c.mm., and subsequent counts gave lower figures. The sample taken on the day after transfusion also showed the maximal number of the normal donor's erythrocytes (Rh-negative), so the concentrations of the two kinds of donor's erythrocytes in this sample were taken to represent 100% survival. The counts of these two kinds of donor's cells in the infant's blood in subsequent samples were expressed as percentages of these maximal figures. It will be noted that (1) elimination of the "nocturnal hæmoglobinuria" erythrocytes was rapid, 50% disappearing in about 12 days; (2) the rate was nevertheless distinctly less rapid than that observed in the adult recipient; and (3) the rate of elimination of the erythrocytes of the normal donor was about 1% a day, a finding which has been shown to be normal for infants (Mollison 1943), provided the figures are corrected for the infant's increasing body-weight (Pickles 1947). The estimates plotted in fig. 1 have been corrected by multiplying them by the infant's body-weight at the time of the test and then dividing them by his body-weight on the day after transfusion.

Tests in Vitro with Normal Serum and Serum from Baby

In each of three experiments the rate and extent of hæmolysis of erythrocytes from the patient with nocturnal

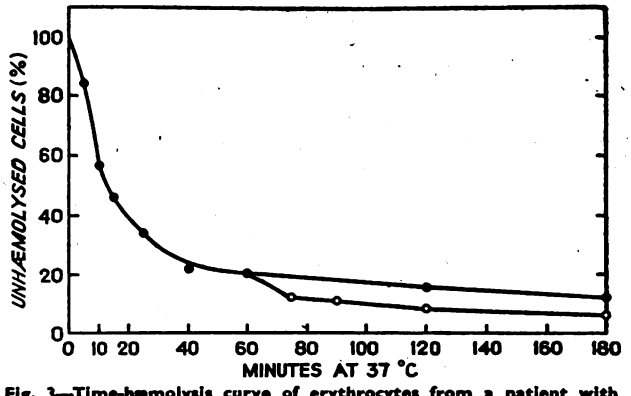


Fig. 3—Time-hæmolysis curve of erythrocytes from a patient with nocturnal hæmoglobinuria in a normal adult serum. After 60 min. the unhæmolysed cells from part of the suspension were resuspended in fresh normal serum. A slight increase in hæmolysis resulted (hollow circles) compared with that produced by the original serum sample (black circles). Hæmolysis was not complete even after 180 min. at 37°C.

Digitized by Google

hæmoglobinuria was notably less—i.e., 9–12%—in the baby's serum than in other sera studied at the same time—i.e., 22–51%. Results of one experiment are plotted in fig. 2. This baby's serum has, in fact, been the least active among a small series of sera of 10 adults and 6 infants studied recently. The hæmolytic activity in vitro of the adult recipient's serum was well within the range of activity of the sera of the other adults.

DISCUSSION

These observations illustrate several aspects of the pathogenesis of nocturnal hæmoglobinuria. First, the erythrocyte abnormality is such that the cells are destroyed more rapidly than normal even in a normal environment. This was expected, particularly in view of the readiness with which the cells are hæmolysed in normal serum in vitro. However, the shape of the elimination curve is interesting (fig. 1*c*); it is steep at first but later flattened. In this respect the curve differs from the more regular "exponential" curves obtained when normal cells are transfused into recipients with idiopathic acquired hæmolytic anæmia (Brown et al. 1944, Mollison 1947).

It may well be more than chance that the present curve (*c*) is so similar in shape to the time-lysis curves of experiments in vitro (figs. 2 and 3). Here too there is a rapid onset of hæmolysis, next a slowing down, and finally a very slow increase in lysis after incubation for 30 min. Complete lysis has never been obtained with the sera used up to now, even when the residual cells remaining after an hour's incubation have been subjected to a further dose of active serum and incubated for another 2 hours. Thus tests in vivo and in vitro both indicate that, as with other types of hæmolysins and hæmolytic systems, there is a remarkable variation in the sensitivity of erythrocytes to hæmolysis. Observations in vitro on the respective sensitivity of reticulocytes and mature erythrocytes do not suggest that the variation is connected with the age of the cells. From the patient's point of view the apparent insensitivity of some of his cells is of obvious benefit.

There was an unexpected and comparatively striking difference between the survival in the two recipients of the cells from the case of nocturnal hæmoglobinuria. The donor's clinical condition and blood findings were essentially similar on the two occasions when blood was collected from him, and it does not seem likely that there was any substantial difference between the two samples of cells transfused. The comparatively slow elimination of the patient's cells in the baby was more probably due to the same factor that caused the relative inactivity of the baby's serum in vitro. Sera vary considerably in hæmolytic power (fig. 2), unpublished observations indicating that the hæmolytic activity of a particular serum as regards rate and amount of hæmolysis is relatively constant for the individual.

It remains to be seen whether the hæmolytic power of the infant recipient's serum was unusually low. A series of observations larger than the present is needed to determine this. However, it may be relevant to recall other reported differences between infant and adult sera. Traub (1943) showed that the complement content of serum, as estimated with sensitised sheep cells, is variable in the infant and is generally less than in the adult; and Witebsky et al. (1947) established that infants' sera, particularly from premature infants, are much less active than adult sera in demonstrating agglutination by incomplete Rh antibodies.

SUMMARY

Blood from a patient with nocturnal hæmoglobinuria was transfused into an adult and into an infant. In both cases the transfused cells were eliminated more rapidly than normal; but the rate of elimination was considerably greater in the adult than in the infant.

The slower elimination of "nocturnal hæmoglobinuria" erythrocytes from the infant's circulation in vivo was paralleled by a notably lower rate of hæmolysis of the same cells in the infant's serum in vitro. The hæmolytic activity of the infant's serum was less than that of 16 other sera from adults and infants.

REFERENCES

Ashby, W. (1919) *J. exp. Med.* 29, 267.
Brown, G. M., Hayward, O. C., Powell, E. O., Witts, L. J. (1944) *J. Path. Bact.* 56, 81.
Dacie, J. V. (1948) *Clin. Sci.* 7, 65.
— Mollison, P. L. (1943) *Lancet*, i, 550.
— Richardson, N. (1943) *J. Path. Bact.* 55, 375.
Mollison, P. L. (1943) *Arch. Dis. Childh.* 18, 161.
— (1947) *Clin. Sci.* 6, 137.
Pickles, M. M. (1947) Dissertation for degree of D.M., Oxford.
Traub, B. (1943) *J. Path. Bact.* 55, 447.
Witebsky, E., Rubin, M. I., Blum, L. (1947) *J. Lab. clin. Med.* 32, 1330.

ŒSOPHAGEAL LESIONS IN SCLERODACTYLY*

W. A. BOURNE
M.A., M.D. Camb., F.R.C.P.
PHYSICIAN, ROYAL SUSSEX COUNTY HOSPITAL AND HOVE GENERAL HOSPITAL

SCLERODERMATOUS lesions of the gastro-intestinal tract first came into notice when Ehrmann (1903) described them in the œsophagus. Such abnormalities have been little discussed in English publications; yet it is fair to say that though they are rare they are likely to be recognisable.

Their rarity is due to the rarity of the sclerodermia group of diseases, which at the highest estimate form only 0·5% of cases in dermatological clinics (Alexander's *Handbuch der Haut-und Geschlechts-krankheiten*, 1927–31, vol. XIV, p. 1), and to the fact that only 5% cause symptoms (Olsen et al. 1945).

The nature of the lesions should, however, be recognised or suspected. Olsen et al. observed that of 350 cases of sclerodermia reviewed at the Mayo Clinic the 18 cases with demonstrable œsophageal changes were associated with one particular manifestation, which has been present in practically all other published cases, including 3 reported by me (Bourne 1947, 1948), and in a fourth now cited here. This is Raynaud's phenomenon progressing to sclerodactyly, the condition of hardened adherent finger tissues with atrophic changes at the tips, which in its fully developed form gives the characteristic radiological appearances of subcutaneous calcinosis and absorption of the terminal phalanges.

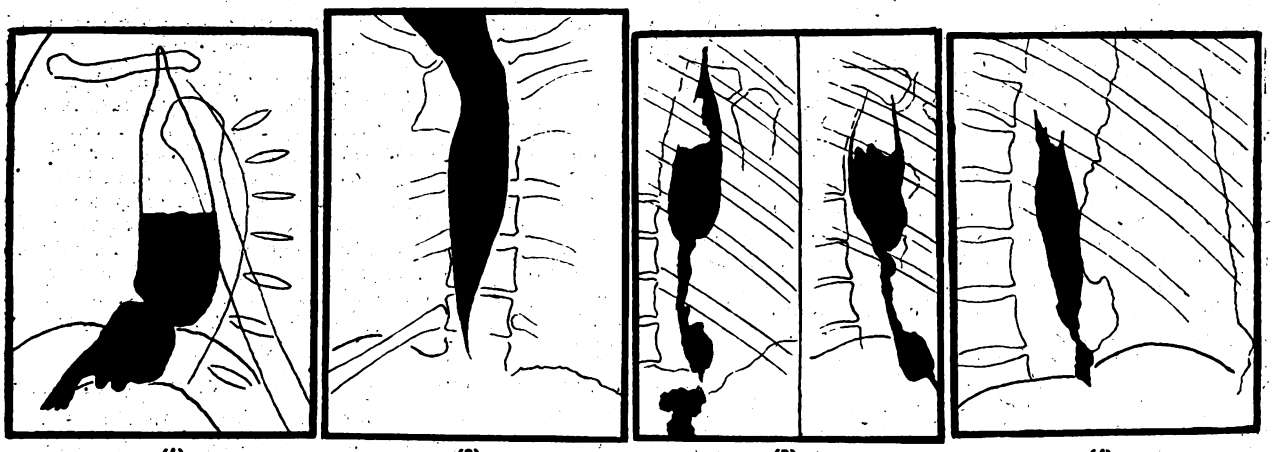
Ehrmann's (1903) original case does not seem to have fallen into this group but to have been of the diffuse type of sclerodermia, in which, as in a case reported by Dowling (1940), the lesions are indefinite, involve the upper rather than the lower œsophagus, and may not be detectable post mortem.

ORGANIC CHANGES

In œsophageal sclerodermia the organic changes vary in site, degree, and extent, but are rare in the upper third. When the cardia is not affected but the œsophagus itself is involved, peristalsis is likely to be abolished and all tone to disappear. The œsophagus then dilates passively when food is taken, until sufficient hydrostatic pressure develops for its contents to enter the stomach. This pressure is not, however, greater than normal, and no symptoms may present except inability to swallow in the horizontal position. So lax may be the œsophageal wall that a common finding in this type of lesion is spontaneous distension with air, presumably from negative intrathoracic pressure, aerophagy, or both. This appearance (Thomas 1942, Kure et al. 1936, Hale and Schatzki 1944) is seen in fig. 1, a tracing from my

* Based on an introduced communication to the British Society of Gastro-Enterologists, November, 1947.

Digitized by Google



(1) (2) (3) (4)

Fig. 1—Tracing of radiogram showing hiatus hernia and œsophagus distended by air.
Fig. 2—Tracing of radiogram showing achalasia of cardia and traction deformity of upper œsophagus due to sclerodermatous pulmonary fibrosis.
Fig. 3—Tracings of radiograms showing narrowing of lower part of œsophagus in a case of sclerodactyly.
Fig. 4—Tracing of radiogram showing obstructive lesion of œsophagus 2 in. above cardia simulating carcinoma.

case 1 (Bourne 1947, 1948), and is probably rare in other conditions.

Fig. 1 also shows another common finding, a hiatus hernia of the short œsophageal type, present in 9 of the 18 cases in the Mayo Clinic series (Olsen et al. 1945), and visible, though not always mentioned, in cases reported by Lindsay et al. (1943), Weiss et al (1943), Fessler and Pohl (1932), and others. Possibly, distension of the œsophagus may facilitate ascent of the cardia by dilating the hiatus. In a case reported by Goetz (1945), however, an active œsophageal ulcer was present. A healed ulcer was found in my case 1 (Bourne 1948), and, since œsophagitis is a common finding (Bevans 1945, Weissenbach et al. 1937, 1938, Rafsky and Herzig 1946), the observations of Allison (1946) on short œsophagus may be relevant and indicate that shortening is produced in these cases as a result of inflammatory fibrosis.

When sclerodermatous change is limited to the region of the cardia, which becomes more rigid, and the hernia is smaller or absent, the changes resemble ordinary achalasia closely, or may be indistinguishable from it except by the associated skin lesions. Fig. 2 shows a tracing of my case 2 (Bourne 1947), reported through the kindness of Prof. J. McMichael, in a patient who had been attending a London teaching hospital for seven years before its nature was recognised on transfer to Hammersmith. It shows also a traction deformity of the upper œsophagus due to sclerodermatous pulmonary fibrosis.

Appearances in the lower œsophagus are more often far less regular and localised. Usually from a third to two-thirds of the lower part is involved (Fessler and Pohl 1932, Hale and Schatzki 1944), but the œsophagus may be narrower than usual throughout its length, or the constriction may involve only 2 or 3 cm., with dilatation above. Fig. 3 shows tracings from my case 4 with characteristic subcutaneous calcinosis, changes in the phalanges, and some years' dysphagia due to persistent œsophageal deformity. Such changes may appear with considerable rapidity, as in my case 3 (Bourne 1947), which Prof. Grey Turner kindly allowed me to cite, in which, following six months' history of Raynaud's phenomenon, dysphagia became severe enough to necessitate gastrostomy and œsophagoplasty. Fig. 4 is a tracing of the radiogram in this case, the report on which was that the appearances were characteristic of carcinoma.

DIAGNOSIS

Diagnosis in such circumstances may clearly be difficult. In advanced cases œsophagoscopy is difficult because of facial rigidity and kyphosis, but in such cases the diagnosis should be clear. When endoscopy has been possible in earlier cases, the œsophageal wall has usually shown leukoplakia or patchy inflammation. Biopsy has not been decisive, since the characteristic histology of sclerodermia elsewhere is not often found. Bevans (1945) reported the mucosal layer of the œsophageal wall to be superseded by fibrillar acellular tissue, with fibrinoid degeneration of the longitudinal muscle, and Goetz's (1945) case showed calcification; but such findings are unusual, and leukoplakia, lymphoid masses (lymphorrhages), polynuclear infiltration, and perivascular collections of round cells are more frequent, as in the cases reported by Weissenbach et al. (1937, 1938) and in my cases 1 and 3 (Bourne 1948).

Intestinal changes may also be present and be demonstrated radiologically (Hale and Schatzki 1944), hæmatologically, biochemically, or post mortem (Bevans 1945, Goetz 1945, and Bourne 1948). Dysphagia of the Plummer-Vinson type may appear as a secondary result. Pulmonary fibrosis has been referred to, and a further viscus affected may be the heart (Weiss et al. 1943, Goetz 1945, Bourne 1948), in which the histology conforms closely with the skin changes in sclerodermia. Indeed, apart from their gastro-enterological interest, these cases are of general importance as showing that sclerodactyly, often distinguished from sclerodermia, is accompanied by visceral changes which prove it to be the same disease.

TREATMENT

Treatment of the œsophageal condition may be unnecessary. If obstruction develops, dilatation may suffice for lengthy periods, as in my case 2 (Bourne 1947) and case 4. When there is serious possibility of carcinoma, thoracotomy is, in my opinion, indicated, as in case 2 (Bourne 1947). The condition is, however, rare, and surgery of the œsophagus is being rapidly developed, with the result that treatment of cases which remain resistant to dilatation cannot at present be laid down. At the Mayo Clinic dilatation by the silk-thread technique has apparently been successful (Olsen et al. 1945).

I am greatly indebted to Prof. J. McMichael and Prof. Grey Turner for permission to cite their cases (cases 2 and 3, Bourne 1947), and particularly to the former for advice and the facilities of his department.

REFERENCES

Allison, P. R. (1946) *J. thorac. Surg.* **15**, 308.
Bevans, M. (1945) *Amer. J. Path.* **21**, 25.
Bourne, W. A. (1947) *Proc. R. Soc. Med.* **40**, 463.
— (1948) *Ibid*, **41**, 43.
Dowling, G. B. (1940) *Brit. J. Derm.* **52**, 242.
Ehrmann, S. (1903) *Wien. med. Wschr.* **53**, 1097, 1156.

Continued at foot of next page

Digitized by Google

ACQUIRED RESISTANCE TO PROGUANIL (PALUDRINE) IN PLASMODIUM VIVAX

D. R. SEATON
M.B. Camb., M.R.C.P.
ASSISTANT PHYSICIAN

E. M. LOURIE
M.B. Lond., M.R.C.P.
DIRECTOR OF DEPARTMENT OF CHEMOTHERAPY

LIVERPOOL SCHOOL OF TROPICAL MEDICINE

Bishop and Birkett (1947) and Williamson et al. (1947) have shown that a strain of *Plasmodium gallinaceum*, maintained by serial blood inoculation in chicks, rapidly develops a high resistance to proguanil ('Paludrine') when repeatedly exposed to subeffective doses of it. Since previous intensive attempts to induce resistance to other drugs in malarial parasites had been unsuccessful, except resistance to pamaquin in *P. knowlesi* in monkeys (Fulton and Yorke 1941), and in view of the wide use of proguanil in human malaria, it became important to determine whether resistance to proguanil could be induced in a species of human malarial parasite.

A strain of *P. vivax* was isolated in April, 1947, from a patient who had contracted malaria in Hong-Kong and never received proguanil treatment. It was then maintained by blood inoculation in two series of patients for whom therapeutic malaria had been prescribed. In the first series the strain was subinoculated from each case *before* proguanil treatment was started in that patient, and repeated observations on this series (in 17 patients) showed that the least amount of proguanil which would regularly stop the fever and parasitæmia within forty-eight hours of the third dose was 1·25 mg. daily on each of three consecutive days. In the second series the subinoculations were, with four exceptions, made *after* the strain had been subjected, in each case, to repeated small doses of proguanil, any increase observed in the minimal effective dose above 1·25 mg. daily for three days being therefore attributable to the development of resistance by the parasites.

The accompanying table shows the progress of the treated strain up to the twenty-eighth passage, about 20 months since its isolation. By the fifth passage there was already a suggestion of slight resistance, which was well established at the eighth passage, and then increased, so that between the twentieth and twenty-fourth passages inclusive (about 14–18 months from the start) 10 mg. of proguanil daily for 3 days had no obvious effect on either the number of parasites or the fever; three doses of 25 mg. invariably failed to clear the blood of parasites, though it reduced their number slightly; and the lowest amount which could clear the blood and stop the fever within forty-eight hours of the third dose seemed to be about 50 mg. daily for three days. Thereafter the resistance increased still further, and at the twenty-seventh and twenty-eighth passages (about 20 months since the start) three daily doses of 100 mg. were without apparent effect on the fever or parasitæmia, though the strain was still sensitive to three doses of 300 mg. This strain may therefore be described as having increased its resistance to proguanil more than eightyfold since the start of these observations.

DR. BOURNE: REFERENCES—*continued*

Fessler, A., Pohl, R. (1932) *Derm. Z.* **63**, 164.
Goetz, R. H. (1945) *Clin. Proc.* **4**, 337.
Hale, C. H., Schatzki, R. (1944) *Amer. J. Roentgenol.* **51**, 407.
Kure, K., Yamagata, K., Tsukada, S., Hiyoshi, J. (1936) *Klin. Wschr.* **15**, 516.
Lindsay, J. R., Templeton, F. E., Rothman, S. (1943) *J. Amer. med. Ass.* **123**, 745.
Olsen, A. M., O'Leary, P. A., Kirklin, B. R. (1945) *Arch. intern. Med.* **76**, 189.
Rafsky, H. A., Herzig, W. (1946) *Gastroenterology*, **6**, 35.
Thomas, E. W. P. (1942) *Lancet*, ii, 389.
Weiss, S., Stead, E. A. jun., Warren, J. V., Bailey, O. T. (1943) *Arch. intern. Med.* **71**, 749.
Weissenbach, R. J., Dechaumes, Martineau, J., Stewart, W., Hoesli, H. (1937) *Bull. Soc. franç. Derm. Syph.* **44**, 1053.
— Boppe, Hoesli, H., Martineau, J. (1938) *Ibid*, **45**, 300.

RETENTION OF RESISTANCE TO PROGUANIL ON PASSAGE THROUGH MOSQUITOES

At the twenty-third passage a batch of *Anopheles stephensi* were fed on case 23b. After they had become infective they were again applied to a patient (not shown in the table) for whom malaria had been prescribed, and who duly developed the infection. Doses of 1·25 mg. and 10 mg. of proguanil, each repeated daily for three days, had no effect on either the parasitæmia or the fever. Higher doses of this general order of magnitude could not be tried, since the patient's condition made it necessary to stop the attack without delay, but it is evident that the resistance to proguanil had survived mosquito-transmission unimpaired.

RELEVANCE TO USE OF PROGUANIL IN ORDINARY PRACTICE

Though more than an eightyfold increase of resistance has been achieved, this work suggests, nevertheless, that the widespread use of proguanil is unlikely to give rise to a serious degree of resistance in strains of *P. vivax* in the field. We produced this resistance under highly artificial conditions, deliberately designed to favour its development and continued for over 20 months, but only during the last few weeks of this period has the resistance risen to doses within the range of those in ordinary use for either suppression or treatment of malaria.

This reassuring conclusion is reinforced by Rollo et al. (1948), who have shown that though resistance to

DEVELOPMENT OF RESISTANCE TO PROGUANIL

Case no.		Weeks since start (on day of inoculation)	Paroxysms* before treatment	Total proguanil (mg.) before subinoculation (main-line cases)	Proguanil (mg.) daily for 3 days	
Main line	Collateral lines				Effective †	Ineffective
1		0	10	0·9		0·3
2		3	4	1·9		0·6
3		5	3	2·2		0·3
	→ 4b	8	1			0·6
4a		7	4	8·7		0·6
5		9	4	25		1·2
6		12	5	nil	1·2	
7		15	10	618·7 ‡	1·2	
	→ 8a	18	5		2·5	1·2
8b		22	4	511·2 ‡		1·2
9a		24	8	11·2		1·2
	9b	20	4		2·5	1·2
	→10b	29	5			2·5
10a		29	5	22·5	2·5	1·2
	→11b	35	7		2·5	1·2
	→11c	41	4			2·5
11a	12b	35	5	21·2		2·5
		43	4			2·5
12a		38	8	11·2		2·5
	→13a	40	3			2·5
13b		41	2	16·2		2·5
	→14b	43	2			5
14a		43	3	65		5
	→15a	46	4			5
15b		46	3	60		5
16		49		nil		
17		53	6	nil	25	
18		54	3	320		25
	→19a	57	10		25	
	→19b	57	7		50	
19c		59	4	700 ‡		25
	→20a	60	6			25
	→20b	62	8			10
	→20c	63	3			10
20d		65	7	15		5
21		68		nil		
	→22a	71	5			25
22b		72	4	75		25
23a		74	7	600		
	→23b	74	7		100	
24		77	1	150	50	
25a		78	2	85		10
	→25b	78	3			10
26		82	2	70		10
27		85	1	185	500	100
28		88	1	1200	300	100

* Defined as occasions on which temperature rose above 100°F.
† Stopped the fever and parasitæmia within 48 hours of the third dose.
‡ In these cases, in addition to treatment with repeated small doses, one or two doses of 250–300 mg. were given during the 36 hours immediately before subinoculation.

Digitized by Google

proguanil can be produced in *P. gallinaceum* by treating infections in fowls during the stage of manifest parasitæmia, it does not arise when the treatment, even though continued daily for as long as a year, is administered during the latent stages—i.e., when the parasites are not demonstrable in blood films. Treatment during latent stages of infection constitutes a very large part of the ordinary clinical use of proguanil in benign tertian malaria, where the drug is given as a suppressive in daily or twice weekly dosage (1) in "prophylactic" regimens, or (2) for a period of, say, six months, to prevent relapse after an acute attack has been controlled. Our experience is that cases of benign tertian malaria are liable to relapse in spite of having completed a six-month course of proguanil at any time up to about two years from the time of the original infection. We have records of several such patients, including one who relapsed on each occasion after three consecutive six-month treatment-courses. In none of these relapses have the parasites failed to respond normally to ordinary therapeutic doses.

SUMMARY

Resistance to proguanil was produced in a strain of *Plasmodium vivax* by giving small doses of the drug to consecutive patients in a series in whom the strain was being maintained by blood-inoculation. The resistance was unaffected by passage through mosquitoes. Though the resistance acquired was more than eighty times greater than normal, it was only within the last few weeks of the investigation that the strain became resistant to doses within the ordinary therapeutic range.

The fact that this degree of resistance did not arise at an earlier stage, though conditions were specially designed to favour its development and were continued for more than 20 months, indicates that the danger of producing a serious degree of resistance in a strain of *P. vivax* by the ordinary use of proguanil in clinical practice is very slight, if not negligible. This conclusion is reinforced, as regards the suppressive use of proguanil, by the recent finding that resistance in fowl malaria cannot readily be produced by treating latent, as distinct from acute, infections.

We are greatly obliged to Dr. A. O. F. Ross, and to Dr. F. Glyn-Hughes and the officers of Belmont Road Hospital for their coöperation in this investigation.

REFERENCES

Bishop, A., Birkett, B. (1947) *Nature, Lond.* **159**, 884.
Fulton, J. D., Yorke, W. (1941) *Ann. trop. Med. Parasit.* **35**, 233.
Rollo, I. M., Williamson, J., Lourie, E. M. (1948) *Ibid*, **42**, 241.
Williamson, J., Bertram, D. S., Lourie, E. M. (1947) *Nature, Lond.* **159**, 885.

STREPTOMYCIN IN NON-GONOCOCCAL URETHRITIS

R. R. WILLCOX
M.B. Lond.
PHYSICIAN IN CHARGE, VENEREAL DISEASES DEPARTMENT, KING EDWARD VII HOSPITAL, WINDSOR; SENIOR ASSISTANT MEDICAL OFFICER, VENEREAL DISEASES DEPARTMENT, ST. MARY'S HOSPITAL, LONDON

PENICILLIN and sulphonamides are not strikingly successful against non-gonococcal urethritis and Reiter's disease, but many of the organisms—e.g., *Bact. coli* and members of the pleuropneumonia-like group—which are thought to be possibly responsible for non-gonococcal urethritis (Harkness and Henderson-Begg 1948), though penicillin-resistant, are susceptible to streptomycin (Powell et al. 1946).

Pulaski (1947) treated six cases of non-gonococcal urethritis with streptomycin and obtained two definite successes and a doubtful one, but he had three failures in four cases of epididymitis.

Kane and Foley (1947) noted clinical and bacteriological improvement in two of three patients in whom only pleuropneumonia-like organisms had been isolated.

Warthin (1948) gave a promising if cautious report of four cases of Reiter's disease treated with 24–28 g. of streptomycin over 6–10 days, but Coodley et al. (1948) reported failure in a single case treated in this way.

The present report covers seven patients, four of whom had a severe and three a mild non-gonococcal urethritis, treated with single intramuscular injections of streptomycin. Though simple bacteriological cultures were performed on the urethral discharges and prostatic secretions of all the patients, no attempt was made to isolate pleuropneumonia-like organisms.

SEVERE URETHRITIS WITH CYSTITIS

Case 1.—A single white man, aged 24, who denied having had sexual contact in the last two months, had a week's history of urethral discharge, dysuria, and hæmaturia. There was a profuse mucopurulent discharge, and the urine was grossly hazy and bloodstained in two glasses. Repeated urethral smears showed no gonococci, and dark-field examination revealed no spirochætes or trichomonads. Urethral culture grew only *Staph. albus*, but *Bact. coli* was cultured from the urine. The Wassermann, Kahn, and gonococcal complement-fixation tests of the blood were repeatedly negative.

On Sept. 13, 1948, the patient was given a single intramuscular injection of streptomycin 0·6 g. in 2 ml. of saline solution. Seven days later not only was there no discharge but also the urine was clear. Five days later still (12 days after treatment) the patient continued well and the prostatic smear showed no pus, though *Staph. albus* still grew on culture of the prostatic secretion. At 19 days after treatment the prostatic culture was sterile, but at 25 days there was a slight relapse of the urethral discharge, though the urine remained clear. At 32 days, however, there was a moderate amount of pus in the urethral smear, the urine was slightly hazy, and *Staph. albus* was again isolated in prostatic culture. The patient was given a further single injection of streptomycin (0·4 g. in 4 ml. of saline solution), and improvement was again immediate, there being no discharge, a perfectly clear urine, and no pus in the prostatic bead 5, 12, 19, 40, 61, and 89 days after the second injection, though *Staph. albus* still grew on prostatic culture.

SEVERE UNCOMPLICATED ANTEROPOSTERIOR URETHRITIS

Case 2.—A single white man, aged 21, had 5 days' history of profuse urethral discharge and slight dysuria. The urine was grossly hazy in two glasses, though no gonococci, spirochætes, trichomonads, or other organisms, were seen in repeated smears and dark-field slides of the discharge. A urethral culture, however, grew coliforms and the ubiquitous *Staph. albus*. The Wassermann, Kahn, and gonococcal complement-fixation tests of the blood were repeatedly negative.

The patient was given a single intramuscular injection of streptomycin 0·6 g., and improvement was immediate. Five days later there was an almost imperceptible meatal moisture, which had passed unnoted by the patient, and a smear of it contained very few pus cells. This moisture, however, had completely disappeared by the 7th day, when no pus was found in the prostatic smear, though prostatic culture still showed *Staph. albus*. The urine was completely clear on both occasions. On examination 11, 21, 28, 33, 55, 84, and 115 days after treatment the patient remained clinically normal, with no discharge, a clear urine, and no pus in the prostatic smears, though *Staph. albus* was still obtained from time to time from prostatic culture.

URETHRITIS, CYSTITIS, AND EPIDIDYMITIS

Case 3.—A single white man, aged 23, who denied having had sexual intercourse in the last two years, had 5 days' history of swollen left testicle with slight hæmaturia. The left epididymis was moderately enlarged, with an acutely tender nodule at the lower pole, and the cord was thickened. A moderate urethral discharge was present, but no gonococci were isolated from it in smear or culture, though coliforms were found in the urine. No trichomonads or spirochætes were observed in the dark field, the urine was very hazy in two glasses, and the Wassermann, Kahn, and gonococcal complement-fixation tests of the blood were repeatedly negative.

Digitized by Google

The patient was given a single intramuscular injection of streptomycin 0·3 g. in 1 ml. of saline solution. Two days later the pain in the testicle had considerably eased and the urine had become clear, though coliforms were still obtained on culture. A week later, not unexpectedly in view of the very small dose given, the cystitis had to some extent relapsed, for the urine was again a little hazy, though the symptoms remained improved. The patient was given a further single intramuscular injection of streptomycin 0·3 g., and 2 and 7 days later the urine was again macroscopically clear, though a few coliforms were obtained on culture. The prostatic smear at this stage was free from pus, and the prostatic culture showed only *Staph. albus*. Two weeks after the second injection, no further measures having been adopted in the meantime, not only was the urine clear and the culture sterile but also the epididymitis was represented only by a just perceptible non-tender residual nodule. The urine and prostatic secretion remained clear, and the patient was symptom-free and clinically normal 21, 28, 35, 63, 79, and 117 days after the second injection.

SEVERE UNCOMPLICATED ANTEROPOSTERIOR URETHRITIS

Case 4.—A single white man, aged 33, who had had unprotected intercourse with a stranger two weeks before, attended with a profuse mucopurulent discharge of two days' duration. No gonococci, spirochætes, trichomonads, or other organisms were detected in the smear or dark field, and the Wassermann, Kahn, and gonococcal complement-fixation tests of the blood were negative. The urine was grossly hazy in two glasses, but culture produced only a few coliforms from the culture and *Staph. albus* from the urethra.

The patient was given a single intramuscular injection of streptomycin 0·3 g. in 3 ml. of saline solution, followed by an immediate reduction of the discharge. When next seen 5 days later there was merely a urethral moisture containing mucus, and the urine was clear, *Staph. albus* alone growing on culture. A prostatic smear taken 2 days later contained no pus. The slight urethral dampness, however, which never assumed the qualities of a gleet, nevertheless persisted for about 18 days before finally disappearing, though at no time did leucocytes reappear in the smear and the urine remained consistently clear. The prostatic smears were repeatedly normal, though *Staph. albus* and *Staph. aureus* were occasionally obtained on culture. The patient remained well 25, 54, 77, and 91 days after treatment.

MILD URETHRITIS AND GLEET

Three white male patients, aged 22–32, were also treated with streptomycin for gleet of 4, 19, and 56 days' duration. One was previously untreated, but two had had sulphonamides, and one penicillin in addition. The discharges were obvious only to the patients in the early morning, there being only a slight mucoid discharge or a mere urethral dampness throughout the day. In each case numerous pus cells, but no gonococci, were observed in early morning smears, and the urine was macroscopically clear but showed a few specks or threads in the first glass. The Wassermann, Kahn, and gonococcal complement-fixation tests were all repeatedly negative, but urethral and prostatic discharges showed *Staph. albus* only in all the patients.

The patients were given single injections of streptomycin 0·2, 0·3, and 0·5 g. Some initial improvement was noted in two, but permanent cures in none. One patient was later given a single injection of streptomycin 1 g. without clinical improvement or bacteriological change.

SUMMARY AND CONCLUSIONS

Seven patients with non-gonococcal urethritis were treated with single intramuscular injections of streptomycin 0·2–1·0 g.

In four patients the signs were severe, with a profuse discharge and/or a grossly hazy urine, and in all of them improvement was immediate and spectacular, though in two cases there was a relapse, which was successfully treated in the same way. Epididymitis was present in one case.

In the three failures the condition before treatment was very mild, with only a minimal discharge and a clear urine with a few threads. The success of streptomycin therapy in this series was thus in proportion to the severity of the condition.

Simple urethral and prostatic cultures were performed in all the cases, and no attempt was made to isolate pleuropneumonia-like organisms. Coliforms were obtained on culture from all four successful cases and in none of the three failures. The urethral *Staph. albus*, which has often been reported in urethral cultures of patients with non-gonococcal urethritis and is probably unconnected with the disease, proved resistant to streptomycin.

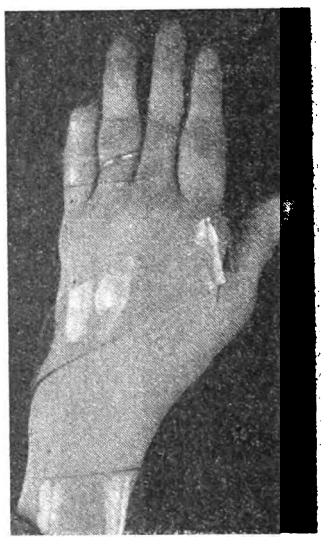
REFERENCES

Coodley, E. L., Weiss, B. J., Egeberg, R. O. (1948) *Ann. west. Med. Surg.* **2**, 500.
Harkness, A. H., Henderson-Begg, A. (1948) *Brit. J. vener. Dis.* **24**, 50.
Kane, L. W., Foley, G. E. (1947) *New Engl. J. Med.* **237**, 531.
Powell, H. M., Jamieson, W. A., Rice, R. M. (1946) *Proc. Soc. exp. Biol., N.Y.* **62**, 8.
Pulaski, E. J. (1947) *J. vener. Dis. Inform.* **28**, 1.
Warthin, T. A. (1948) *Amer. J. Med.* **4**, 827.

New Inventions

PERSPEX SPLINT FOR ULNAR-DEVIATION OF THE FINGERS

A WIDE variety of appliances have been devised to deal with the crippling deformity of ulnar deviation of the fingers which commonly accompanies rheumatoid arthritis. No single method has held the field for long, mainly because the maker of the appliance has concentrated on producing an anatomical rather than a functional cure; the patient then finds that she is no better off when wearing it, and so abandons it. Another objection to most appliances is that they are cumbersome; while female patients find them unsightly.



We have tried to overcome these objections in the splint here illustrated. A plaster-of-paris cast is made of the patient's hand; then a strip of 'Perspex,' 1 in. wide and about 18 in. long, is warmed until soft, wrapped round the cast, and allowed to cool. The splint is light, is not unsightly, and permits almost normal use of the hand. It possesses considerable spring and is quite easily put on and taken off with a little practice. The appliance is intended for prophylactic use as well as for the established deformity.

It is a pleasure to acknowledge the help we have received from Sister F. L. Greenhill, Miss C. E. Barraclough, Sister M. Latimer, and several members of the staff of the unit.

C. B. HEALD, M.D.
BRANDON LUSH, M.B.
J. F. BUCHAN, M.B.

Rheumatology Unit,
Royal Free Hospital.

"... To make a successful postgraduate school it is necessary for most of the surgical staff to undergo a rebirth. They must say farewell to the day when surgical reputations were built solely on knowledge and skill and accept a new standard of excellence which is based on the quality of the men and women they have trained."—Prof. W. E. GALLIE, F.R.C.S., in the eighth Listerian Oration (*Canad. med. Ass. J.* 1948, **59**, 201).

Digitized by Google

Reviews of Books

Hæmolysis and Related Phenomena

ERIC PONDER, Nassau Hospital, Mineola, N.Y. London: J. & A. Churchill. 1948. Pp. 398. 50s.

THIS monograph by an acknowledged expert is an essay in biophysics and as such is of more interest to physiologists than clinicians. In all sections a fair knowledge of physics and mathematics is needed by the reader, since the treatment is mathematical whenever possible. The first chapters deal in minute detail with the structure and cytochemistry of the red cell; later chapters with the kinetics of hæmolysis, and with inhibitor-accelerator systems. These systems have attracted the attention of clinical workers in the last few years since it has been suggested that hæmolytic episodes like those in blackwater fever may be due more to unbalancing of these systems than to the presence of undetectable hæmolysins; the reader will find here a full discussion of these difficult conceptions. The final chapter on hæmolysis in vivo collates all the recent work on red-cell survival and the attempts to demonstrate hæmolysins; the various clinical hæmolytic syndromes are outlined here. Two appendices give information, not to be found elsewhere, about the properties of the peculiar red cells of camels and the nucleated red cells of the lower vertebrates; a third tells us once more how inaccurate, statistically, our methods of red-cell counting are; and a fourth gives original information—some provided by Dr. C. O. Warren—on red-cell metabolism.

This, then, is a full but not unreadable discussion of a subject which reaches "the limits of knowledge." We are glad to see that a "selective" bibliography is provided instead of an immense "complete" one; even so there are 12 pages of references which Ponder considers serious students of the subject should know about, if they are not "to find themselves in a shaky position as regards fundamentals."

Juvenile Rheumatism

G. E. M. SCOTT, M.B. Melb., medical clinical assistant, Royal Melbourne Hospital. Melbourne: W. Ramsay (Surg.) Pty. 1948. Pp. 163. 25s.

THIS monograph is largely a review, with original comments, of comparatively recent literature. Over 97% of the 235 references are in Anglo-Saxon, and many of these are second-hand; e.g., "In a review of juvenile rheumatism in London in 1939, P. S. Hench et alii . . . ." Interspersed are 31 original case-records of rheumatic fever and observations thereon, as well as two tables and one figure illustrating the age at onset in 645 patients seen at the Children's Hospital, Melbourne, between 1936 and 1942. A few other statistics on this series are given.

The Practice of Group Therapy

Editor: S. R. SLAVSON, director of group therapy, Jewish Board of Guardians, New York. London: Pushkin Press. 1948. Pp. 271. 21s.

PSYCHIATRISTS often advocate group therapy on the ground that it permits several people to be treated at once by the psychotherapist, whose methods in any case take a lot of time. Such supporters think individual treatment better, when it is practicable; but they are ready to make a virtue of necessity, and find some advantages in group treatment. They are also generous in giving this name to a wide variety of methods, ranging from those of discussion groups and social clubs to "psychodrama." The contributors to Mr. Slavson's symposium are not of this sort. They are whole-hearted in their belief that group treatment has great intrinsic value, which makes it much more than a substitute for individual treatment; they expect it to bring about more or less permanent modifications within the patient's personality; and they limit the term to the treatment of a small, specially selected group. Their terminology and theory are largely borrowed from psycho-analysis; one of them, Dr. N. Ackerman, a prominent New York psycho-analyst, says that "group psychotherapy, operating on an interpersonal level different from that in psychoanalysis, yet gains much from applying psychoanalytic insight to the dynamics of group living. On the whole, Group Therapy is a more real experience than is individual therapy. It is less bound to the irrationalities of the unconscious and is weighted on the side of social reality."

The book deals with "activity group therapy," applicable to children, and "interview group therapy" for adolescents and adults. Neither of these is radically new, and much of the discussion is inflated with wordy intimations of the obvious. The case-records, however, which constitute the bulk of the material in the book, show how much can be done by a group therapist who has good judgment, restraint, and a clear purpose.

Streptomycin und Tuberkulose

Editors: G. FANCONI; W. LOFFLER. Basle: Schwabe. 1948. Pp. 357. Sw. fr. 30.

IT is understandable that the literature on streptomycin should multiply rapidly, since it is the first drug to influence to an important degree the course of tuberculosis in human beings. This book is a collection of reports by Swiss authors, with good illustrations and a fairly comprehensive bibliography.

Separate articles cover the experimental basis for streptomycin treatment, the cytotoxic action of streptomycin, and its effect in experimental tuberculosis, in miliary and meningeal tuberculosis in human beings, in childhood tuberculosis, and in tuberculosis of the lungs, tracheobronchial tree, eyes, and urogenital system. Dolivo and Rossi compare results of three methods of treatment of meningitis, but the numbers are very small and the series were observed for different periods of time. Tanner reports the results of intracavitary injection of streptomycin in 11 cases; he considers this method has its chief value as a preparatory measure for surgery. There is a chapter on the vestibular effects of streptomycin therapy, and a particularly interesting one by Zollinger on pathological findings in 22 cases of tuberculous meningitis treated with streptomycin. He reports evidence of considerable healing of tuberculous lesions and believes that much of the failure is due to vascular lesions; to be effective, streptomycin treatment must start before diffuse exudation and vascular lesions are established. He finds no proof of a special type of healing under streptomycin treatment, and believes that the drug, by bacteriostatic action, enables the body to mobilise its reaction to the tubercle bacillus in time.

Very little work on streptomycin sensitivity is reported, and the book, while presenting attractively different aspects of streptomycin treatment, adds little to what is already known.

A-B-C's of Sulfonamide and Antibiotic Therapy

PERRIN H. LONG, M.D., F.R.C.P., professor of preventive medicine, Johns Hopkins University. Philadelphia and London: W. B. Saunders. 1948. Pp. 231. 17s. 6d.

THIS little book is a handy compendium of an important subject, well written and easy of reference since it is arranged alphabetically. The subject matter is up to date, including such comparative novelties as caronamide. (The transient renal damage caused by this drug might have been mentioned, and also its value in the treatment of bacterial endocarditis.) A few selected diagrams would have conveyed more to the eye and memory than several pages describing the blood levels achieved and maintained by giving various doses of penicillin by different routes. Also, a table setting out the relative solubilities of the acetyl derivatives of the various sulphonamides in urine of different pH levels would have given some idea of the dangers of crystalluria with various compounds, and might well have been supplemented by a figure comparing the excretion-rates of different sulphonamides before and after acetylation. Oral administration of penicillin is mentioned on two occasions: on the first Professor Long emphasises the part played in its destruction by acid in the stomach, though on the second he makes it clear that this is relatively unimportant as a cause of the poor blood levels attained when penicillin is given by this route. The importance of regular white-cell counts when sulphonamides are being used in heavy dosage in severe infections might have been emphasised. The book will be useful to the busy practitioner, but—in the absence of plates and figures—it is rather expensive.

Digitized by Google

Glomerular Nephritis

Diagnosis and Treatment. THOMAS ADDIS, M.D., F.R.C.P.E. London and New York: Macmillan. 1948. Pp. 338. 40*s*.

Dr. Addis directs a large clinic for renal disease, and has devised many simple and ingenious methods for observing and controlling the progress of his patients. Although he says that his book has been written because "the present day treatment of patients with renal disease is inadequate and sometimes dangerous," only the final chapter deals with practical problems of treatment. After reading the discussions on the relation of renal mass to function, and on the significance of the various clinicopathological investigations in renal disease, it is difficult to know whether to be pleased or disappointed to find that the treatment advocated approximates closely to what is usual in this country. The book will be read for two main reasons: (1) for the exposition of the author's views on the diagnostic value of careful microscopy of the urinary sediment; and (2) for the full and lucid account of his and his colleagues' work on renal function and the hyperplasia of surviving renal tissue. It is based almost entirely on clinical and experimental observation, and is therefore a welcome addition to renal literature.

Physiology of the Eye

HUGH DAVSON, D.SC., honorary research associate, University College, London: formerly associate professor of physiology, Dalhousie University, Canada. With a foreword by Sir Stewart Duke-Elder. London: J. & A. Churchill. 1949. Pp. 451. 32*s*.

AN up-to-date book on eye physiology was overdue, for none has appeared in this country since 1938, when Duke-Elder's vol. I contained a section on this subject. Dr. Davson has for many years been a lecturer on physiology and physiological optics to medical students and postgraduates taking their D.O.M.S., and no-one knows better the need of a fairly small and concise textbook to help them. He recognises also that medical men are usually intimidated by complicated mathematical formulæ and that they only need to know enough of optics to follow the rationale of the techniques they employ. The text is divided into five sections, on intra-ocular dynamics, mechanism of vision, muscular mechanisms, visual perception, and optics; and the subject matter is standard teaching and non-controversial. Modern trends are introduced, such as the electroretinogram and Granit's experiments on colour-vision. The author has a clear and easy style, and realises that he is speaking to clinicians rather than scientists; and his book therefore achieves its exact object of teaching the fundamentals of eye physiology to those doctors who are aware of its importance and wish to know more.

Psychology of Personality

(2nd ed.) ROSS STAGNER, professor of psychology, Dartmouth College. New York and London: McGraw Hill. 1948. Pp. 485. 30*s*.

THE sophisticated reader would fifteen years ago have shied away from a book with this title as sharply, and for the same reasons, as if it had been called "How Your Mind Works." Such aversion is no longer warranted or common; normal personality has become one of the most lively fields of scientific investigation in psychology. The present volume is a well-organised, mildly critical survey of the extensive material now accumulated. After describing the techniques used for studying personality in respect of the subject's effect on others, his consistent responses, and the inner systems which constitute the deeper level of his personality, Professor Stagner examines its development from childhood to maturity, and the major traits which can be detected in the organised personality; chapters on the self, character, attitudes and values, expressive movements, and type theories of personality conclude this descriptive section. The other half of the book is concerned with the dynamics and determinants of personality; here the author's bias is towards the social rather than the constitutional factors. The family, the school, and the economic and cultural influences which determine personality are for him of at least equal importance with the biological and intrapsychic forces which psycho-analytic theory emphasises. He likes Kurt Lewin's concepts of valence and tension in motivation, and many passages show how readily he has adopted, and occasionally adapted, Lewin's mode of thinking. The result is a kindly, selective book, which would perhaps be better if it had a little salt and sting, so valuable for helping the reader to discriminate among a host of theorists and observers. The size of this host is shown by the admirable bibliography, which includes some 600 items. Doctors who suppose that Freud and Jung and the novelists have said all there is to say so far about personality will profit by letting themselves be introduced to this larger company by Professor Stagner.

Experimental Diabetes Mellitus

E. T. BELL, M.D., department of pathology, University of Minnesota. Oxford: Blackwell Scientific Publications. 1948. Pp. 31. 7*s*. 6*d*.

THIS short but superbly produced monograph on the four types of experimental diabetes deals mostly with alloxan diabetes. The writing and sections are logically arranged, but it does not set out to be a comprehensive reference book. Unfortunately black-and-white photomicrographic reproductions of alpha and beta cells and their granules are much less informative than they would be in colour.

Youth in Despair

RALPH S. BANAY, M.D. New York: Coward-McCann. 1948. Pp. 239. $3.

Dr. Banay has a capacity for absorbing statistics, reports, technological data, and odd scraps of significant conversation, while remaining human, balanced, and undismayed by the Augean stables he is studying. Much work has gone to the making of this critical survey, complete with constructive suggestions, of the problem of juvenile delinquency in the United States—its cause, its clinical picture, and the methods available and adopted (often quite different things) for dealing with it. And he has compressed all this into a short book. Unfortunately perhaps, the standard he asks for an adequate solution of the problem is so high that a reader with a practical mind may be forgiven a sigh. For a long time yet, hard-working psychiatrists will be doing jobbing carpenters' work in society, combining some technical knowledge with wit and ingenuity and good will, coping with conditions heavily loaded against them. Nevertheless they should read Dr. Banay's book.

Blood Clotting and Allied Problems (New York: Josiah Macy Jr. Foundation. 1948. Pp. 179. $3.25).—This is the verbatim record of the first conference of the foundation, held a year ago. Most of the original material has now been published in the journals; but it is useful to have it in this form, and to see the comments of the other workers at the meetings. A series of instructive charts by Irving S. Wright show the prothrombin concentrations of patients taking dicoumarol over long periods, estimated by the one-stage and two-stage methods, and sometimes by the diluted-plasma method. Another interesting section gives the actual techniques of prothrombin estimation used in eight different schools in the United States and Canada. The booklet provides up-to-date information for "coagulationists."

Therapeutic Uses of Infra-Red Rays (4th ed. London: Actinic Press. 1947. Pp. 149. 15*s*.).—Dr. W. Annandale Troup applies infra-red rays to a very wide range of disorders. These include "any painful condition"; diseases which have caused muscular wasting, such as anterior poliomyelitis and facial palsy; leukæmia (in which he states it has been used "successfully," though apparently in only one French case, of which no details are given); frostbite; endarteritis obliterans; X-ray dermatitis; sinusitis; pharyngitis, laryngitis, and otitis media; gingivitis; acute and chronic sprains; postoperatively for patients with acute abdominal conditions; paralytic ileus (which it "relieves"); and, of course, rheumatic conditions. That infra-red rays (like any other source of heat) cause hyperæmia of the treated part, and relieve pain in the nerve-endings, nobody will deny; but Dr. Troup's enthusiasm raises it almost to the status of a panacea. His zeal outruns his discretion.

Digitized by Google

THE LANCET

LONDON: SATURDAY, MARCH 5, 1949

Death Among The Newborn

MIDWIFERY [1] and maternity [2] in Great Britain have lately been well scrutinised; and now a joint committee of the Royal College of Obstetricians and Gynæcologists and the British Pædiatric Association, with Sir EARDLEY HOLLAND as chairman, have reported to the Minister of Health on "Neonatal Mortality and Morbidity." [3] There is evidence, they assert, that the present neonatal mortality and stillbirth rates could be reduced by as much as a third or even a half; which would mean a saving of some 15,000 babies yearly in England and Wales. The two great preventive measures which pace each other throughout their report are, first, better nutrition and conditions of life for mothers, and, secondly, better obstetrics. These two measures may roughly be related to a long-term and a short-term policy.

Good feeding and good conditions of life fit the mother for childbearing in both general and special ways. Poor feeding, and especially fat deficiency, increases the incidence of contracted pelvis, a potent hazard for the child. Diseases of the placenta and membranes associated with accidental hæmorrhage and infarction mainly arise when the mother is suffering from toxæmia, and prematurity and intracranial hæmorrhage in the child are also commoner in toxæmic pregnancies. Though the origin of toxæmia is not understood, there is reason to think that a sound diet and good living conditions help to prevent it. Failure of lactation is favoured by nutritional anæmia: women in poor circumstances with a hæmoglobin reading of under 70% did not maintain breast-feeding as long as women in better social circumstances with a higher hæmoglobin level; moreover, severe anæmia during pregnancy was shown to be associated with a high sickness-rate among the children. Breast-fed infants survive more often than those who are artificially fed: and only the properly nourished mother can breast-feed her child properly.

As a long-term policy, then, we should be able to reduce the neonatal mortality in years to come by building up a race of well-nourished young women, living in a healthy way. Our short-term policy must be to ensure that the mothers are skilfully delivered, and that children are protected from careless management in their early days. Even beneficent obstetric measures may be harmful when misapplied. The committee note that "analgesics and hypnotics, when properly employed, may facilitate the progress of natural labour by relieving pain and allaying the mother's anxiety, and may thus afford a certain degree of protection to the child." On the other hand, anæsthetics and analgesics, used less well, may prolong labour and make operative delivery necessary, thus increasing the risk of asphyxia or birth injury. The latter is still one of the leading causes of stillbirth and neonatal death. In a post-mortem study of 800 infants under 4 weeks of age J. N. CRUICKSHANK [4] in 1930 found that death was due in 67% to asphyxia neonatorum, prematurity, or birth injury. When asphyxia and head injury occur together it is hard to decide which is the primary factor: head injury leads to asphyxia, and asphyxia promotes hæmorrhage. But birth injury is estimated to be responsible for a quarter to a third of all neonatal casualties, and for a quarter of all cases of intranatal death. The injury may be directly due to the use of instruments, or indirectly due to errors of judgment which expose the child to undue stress in its passage down the birth canal. Obstetric manipulations, breech delivery, and vigorous methods of resuscitation may also endanger its life—the risks being of course increased if the child is premature or anoxæmic. That the skill of the obstetrician may turn the scale is not perhaps sufficiently appreciated. The committee note that "breech delivery in primigravidæ still causes, in many hospitals, a fœtal mortality, mainly due to intracranial injury, of 20 per cent. or more. It has been demonstrated that this figure can be lowered to 3 or 5 per cent. by good obstetric technique alone." This statement is perhaps the best-placed shaft the committee loose. It shows that, despite three recent instructive reports relating to the nation's maternity service, we are not yet fully informed. We still need an analysis of the obstetric teaching given to medical students in the various medical schools of the country, a study of the experience in obstetrics of those now entering general practice and engaging to do midwifery, and an examination of the obstetric results obtained by representative practitioners in various parts of the country.

The committee suggest some useful measures for the better protection of the newborn child. Human milk, gentle handling, and protection from infection are its main requirements. They advocate the establishment of milk banks, special nursing care for premature infants, and early repeated transfusions with Rh-negative blood for the baby with hæmolytic disease. Some far-reaching recommendations on the arrangement of maternity units are likely to flutter the dovecots, but they would obviously prevent much cross-infection. The common "changing-room" and transport trolleys have had their day. Babies should be changed at the cotside, and soiled napkins should be dropped into a special container and not be touched again by any nurse. Destructible napkins should be used when possible, and the floors of nurseries should be treated to reduce the risk of dust infection. Each baby should have a separate bath, and should have no more than two or three baths during his first fortnight of life: "frequent bathing may damage the baby's skin and predisposes to skin infection." A doctor's and a nurse's gown should be provided for every cot, and all in attendance should wear masks

1. Report of the Working Party on Midwives. See *Lancet*, Jan. 29, p. 190.
2. Maternity in Great Britain. London, 1948. See *Lancet*, 1948, ii, 813.
3. *Rep. publ. Hlth med. Subj., Lond.*, no. 94. London: H.M. Stationery Office. 1949. Pp. 92. 1s. 6d.
4. *Spec. Rep. Ser. med. Res. Coun., Lond.*, no. 145, 1930.

Digitized by Google

and be proficient in mask drill. Propaganda about infection should be intensified and maintained, and an "infection conscious" outlook should be fostered in junior nurses (and, surely, in medical students) by lecturers, sisters, and staff nurses. Routine swabbing of the throats of the staff and ward-maids would make it possible to exclude those carrying pathogenic organisms. These and the other straightforward measures of modern hygiene set out in the report should now be accepted as a routine in every maternity unit. They are a nuisance to carry out, but so is aseptic surgery. The time has come when it is as culpable to ignore the one as the other.

Hodgkin's Disease

THE introduction of a new treatment for any disease commonly leads to a re-examination and refining of our ideas on its diagnosis as well as its prognosis. This is true of Hodgkin's disease, for which the nitrogen mustards and radioactive isotopes are now on trial. Radiotherapy affects Hodgkin's disease and some other clinically similar diseases, like follicular lymphoblastoma, in much the same way; but these newer treatments are more selective in their action, so diagnosis must be correspondingly more precise. Three reviews that have lately appeared will help those who wish to brush up their knowledge of this subject. HOSTER and his colleagues [1] survey every significant paper on the diagnosis, prognosis, treatment, and ætiology from 1832 to 1947, but their uncritical collection of often contradictory facts may well bewilder the reader. SYMMERS'S [2] shorter review deals with the whole field of lymphoid diseases; it gives much more information about the differential diagnosis of Hodgkin's disease; but is also mainly a list, though the author's views are clearly expressed. The monograph by JACKSON and PARKER [3] provides a bird's-eye view of the disease, based mainly on their own material.

Hodgkin's disease is rarely localised; it affects the lymphatic system as a whole, even though enlarged cervical nodes are the first presenting sign in about half the patients. By the time these nodes are large enough to worry the patient the mediastinal and abdominal nodes are almost certainly affected; necropsies show that in most cases the typical changes of Hodgkin's disease are there, particularly in the clinically inaccessible retroperitoneal and para-aortic nodes. Sooner or later most organs are involved, the first being spleen, liver, and bones—especially vertebræ (23% in the series reported by JACKSON and PARKER). The disease has been classified on clinical and on pathological evidence. GILBERT [4] distinguished four clinical types: (1) an average form (60% of cases) beginning with a local enlargement of lymph-glands extending by a series of exacerbations and remissions involving lymphatic tissue all over the body, and ending in cachexia or secondary infection; (2) a slow form (20%), gradually spreading over many years, with long remissions independent of treatment; (3) a rapidly extending form, resistant to treatment, which kills by visceral complications rather than by cachexia; and (4) the rare acute form in which there is high fever, all the lymph-nodes seem to enlarge at the same time, and the patient lives for a few weeks at most. JACKSON and PARKER divide cases into three classes according to the histological appearances of the glands: (1) Hodgkin's "paragranuloma," in which the structure of the gland is more or less disturbed but the predominating cell is still the lymphocyte, and the typical Sternberg-Reed giant cells can always be found if looked for; (2) Hodgkin's "granuloma," corresponding to the classical type with giant cells, proliferation of eosinophil and reticulum cells, and varying fibrosis; and (3) Hodgkin's "sarcoma," in which the whole gland is replaced by a fairly uniform proliferation of large cells with multilobed nuclei. The paragranuloma is localised and progresses very slowly. After many years it can turn into the granuloma phase—for example, a patient who had some enlarged cervical nodes removed by block dissection in the paragranuloma stage developed typical Hodgkin's granuloma 19 years later and died within 3 years. The Hodgkin's sarcoma is rapid, attacks visceral more often than superficial lymphatic tissue, occurs at a later age, and is inevitably fatal. JACKSON and PARKER'S classification has its critics—thus the histological distinction between paragranuloma and granuloma is not always clear, and some regard the Hodgkin's sarcoma as a separate type of reticulosarcoma—but it roughly corresponds to the different clinical types, and their figures for survival are important as exemplifying the standard by which new forms of treatment must be judged. These figures show that in Hodgkin's paragranuloma 55% of the patients survive 5 years or more, and some have lived for 30 years or so after diagnosis. In Hodgkin's granuloma 24% die in the first year, 45% within 2 years, and only 13% survive over 5 years; in a group of 90 patients treated by radiotherapy the average survival was 2·7 years. Of the patients with Hodgkin's sarcoma 30% died within 6 months and none survived 2 years.

Before prognosis can be assessed and treatment decided on, the type of disease must therefore be known. Diagnosis on the basis of symptoms and signs is aptly described by SYMMERS [2] as "an interesting, if precarious venture." There are too many similar syndromes for clinical observation alone to be reliable. A biopsy of a properly chosen lymph-gland, properly stained and fixed by regular methods, is essential; and, since different lymph-nodes may show different stages of development, more than one biopsy may be needed.[5] Aspiration biopsy has been recommended [6] but is not yet popular. When treatment is to be considered, JACKSON and PARKER emphasise an important principle: those in charge "must constantly be on the look-out for evidence of involvement of internal organs and must not content themselves with gratifying results of treatment directed solely to superficial lymph nodes, which are in most cases merely the visible expression of an internal lesion." It is because X-ray treatment has been mainly directed to local lesions, and has not been well adapted to treatment of the whole body, that so much interest

1. Hoster, H. A., Dratman, M. B., Craver, L. F., Rolnick, H. A. *Cancer Res.* 1948, **8**, 1.
2. Symmers, D. *Arch. Path.* 1948, **45**, 73.
3. Jackson, H. jun., Parker, F. jun. Hodgkin's Disease and Allied Disorders. New York, 1947.
4. Gilbert, R. *Amer. J. Roentgenol.* 1939, **41**, 198.
5. Slaughter, D. P., Craver, L. F. *Ibid*, 1942, **47**, 596.
6. Hermittc, L. C. D., Ellis, F. Recent Advances in Clinical Pathology. London, 1947; p. 324.

Digitized by Google

attaches to the newer treatments that overcome this difficulty. Since the use of nitrogen mustards was discussed in these columns [7] 18 months ago, no large series of cases of Hodgkin's disease has been reported. WILKINSON and FLETCHER [8] had good results in 3 out of 4 patients with the longest observation of 17 weeks. ZANES et al.[9] have given data about 31 patients treated with methyl-*bis*(β-chloroethyl)amine; the average remission was 2·8 months and the longest 6 months; 10 patients have died; 8 who were classed as resistant to radiotherapy responded to nitrogen mustards. These results are encouraging, but it will be some time before we can say that this treatment produces the same order of survival as radiotherapy has done. Of the radioactive isotopes, phosphorus (P^{32}) has proved disappointing. HAHN and SHEPPARD [10] reported reasonable results with radiomanganese, but these results have not been followed up.

On the whole, therefore, the chloroethylamine drugs offer the most promising line of research in the treatment of Hodgkin's disease, and attempts are being made to overcome their disadvantages, especially the necessity for intravenous injections and the distressing vomiting that follow their use in many patients. In assessing results the recent reviews emphasise the necessity of eliminating from the treatment series the slowly progressive forms whose survival-times will be long even without treatment.

Bacterial Warfare

THE spontaneous interference of bacteria in the course of history is exemplified so often in military annals that it is not surprising that the possible offensive use of microbiological agents has often been considered. Between the wars French authors in particular discussed the project in detail. On what has been thought and said since 1939 our information comes chiefly from two publications by Dr. ROSEBURY and his colleagues in the United States. The first [11] is in the nature of a survey of possibilities, written in 1942 and kept under secret cover till 1947. The authors admit that more recent work has made much of their report of no more than historical interest, but it retains some significance. The organisms causing disease in man, animals, and plants are reviewed in the light of certain criteria thought to define their potentialities as weapons of offence—infectivity, casualty effectiveness, availability, means of transmission, possibilities of detection and defence, and "retroactivity" (danger to the users). Many of the more obvious methods by which disease might be spread among the enemy are clearly impossible on a scale likely to be of offensive value. (The masked agent throwing "germs" into the public reservoir of Little Gasping on a dark night must be left to fiction and the village gossips.) History suggests that the diseases with a rapid epidemic spread should be most effective weapons; but it is seldom easy to apply the spark that sets an epidemic in train. If rats infected with plague, or mosquitoes bearing the virus of yellow fever, are dropped from aeroplanes, they will not necessarily start an epidemic. In many parts of the world man lives among animals endemically infected with *Pasteurella pestis*; yet human infection is only sporadic. *Aedes ægypti* is found throughout the tropics, but it seems that the coöperation of some genius loci is necessary to spread yellow fever. The truth is that we are still ignorant of the factor necessary to precipitate epidemics of the major infectious diseases, and that, until this ignorance is dispelled, attempts to employ them in war are likely to be as hazardous for the user as for the victim—or as inoffensive. Against many of the diseases, such as typhoid fever and cholera, whose epidemic history is simple enough to give some promise of success, we have reasonably effective methods of prophylaxis. Such protection is lacking against bacillary dysentery, but prevention by other means is simple except under conditions of chaos. The use of such infections as psittacosis, virulent influenza, and poliomyelitis is limited by our ignorance of methods of dispersal, while most diseases of protozoal origin seem to be insufficiently noxious. The diseases of domestic animals have lost their terrors for the transportation services, though they might be used to diminish food-production. Perhaps the most likely chance of a successful epidemiological offensive lies among the diseases of cultivated plants. The death of every potato plant would go far to defeat any country in the temperate zone.

Another way of using micro-organisms or their toxins would be to apply them to missiles, whose effect would then be lethal even if they caused only slight wounds. The exotoxins of *Clostridium botulinum* and *Corynebacterium diphtheriæ* have powers beyond a Borgia's dream, and a strain of *Bacillus anthracis* rendered resistant to the commonly advertised chemotherapeutic agents might prove exceedingly harmful if introduced into the tissues with an adjuvant such as calcium chloride or quartz. ROSEBURY has suggested that if the virus of psittacosis, for example, were incorporated in a toxic smoke its power of infection might be enhanced; and experimental investigation of the possibilities of such methods is the subject of his book.[12] This, though the words never appear in the text, is in fact a primer of bacterial warfare. It is a highly technical account of the working of a small plant designed for investigating the stability of bacterial clouds and their infectivity for laboratory animals. The pathogenic organisms tested were representatives of the genera malleomyces, pasteurella, and brucella, and viruses of the psittacosis group. The findings are of little general interest and it is not a work to be recommended to the sensation-monger. That it should be published at all may strike some as odd; but careful study shows that it is unlikely to be of much value to an enemy, while the details of plant operation might be useful for other purposes.

The experiments that ROSEBURY records came to an end in 1945; but nobody can doubt that the ideas behind them have been further pursued since then, not only in the U.S.A. but probably in every country where there are some petri dishes and nutrient agar.

7. Leading article, *Lancet*, 1947, i, 914.
8. Wilkinson, J. F., Fletcher, F. *Ibid.*, ii, 540.
9. Zanes, R. P., Doan, C. A., Hoster, H. A. *J. Lab. clin. Med.* 1948, 33, 1002.
10. Hahn, P. F., Sheppard, C. W. *Sth. med. J.* 1946, 39, 558.
11. *J. Immunol.* 1947, 56, 7.
12. Experimental Airborne Infection. By Theodor Rosebury. Baltimore, 1947.

Digitized by Google

Two years ago in Copenhagen the following resolution was passed :

> " The Fourth International Congress of Microbiology joins the International Society of Cell Biology in condemning in the strongest terms all forms of biological warfare. The congress considers such barbaric methods as absolutely unworthy of any civilised community and trusts that all microbiologists throughout the world will do everything in their power to prevent their exploitation."

How many resignations, we wonder, has this resolution caused ? The dilemma before those engaged in investigations applicable to bacterial warfare is much the same as that confronting the far larger number involved in research on atomic fission. The fact that knowledge may be an ignis fatuus, or worse, has never yet halted man in its pursuit : empty the inkwell, burn the paper, and lop off his hands—the mind will go on seeking and searching. To scientists, however, this carries the corollary that their knowledge is for all the world ; and many today are deeply troubled by governmental injunctions to secrecy. The process of civilisation is undoubtedly reversed when scientific workers, whether in Russia or England, acquiesce in political direction in time of peace. Very often at least, their willingness to do so can be explained only by the fact that there is as yet no true peace : in every country people still feel that not only their " way of life " but their very lives are in danger. Few now put much faith in treaties or conventions either for preventing war or for mitigating its horrors ; we have become accustomed to the idea of total war in which the combatants believe that so much is at stake that they can stop at nothing that would gain them advantage. Where there are few neutrals, the opinion of the outside world about broken conventions is of little immediate importance, and such conventions are likely to be broken unless the other side is in a position to retaliate : for example, we probably owed our recent immunity from chemical warfare to the excellence of our offensive preparations.

At one time the rules of war gave it some of the characteristics of an elaborate game played by civilised people. Perhaps it might have developed along these lines into an international sporting contest. But its actual development has been in the opposite direction, into a struggle where necessity knows less and less law. Where defensive and offensive operations are no longer separated, and war is deliberately waged on nations rather than their armies, the chance of ruling out particularly horrible weapons or practices becomes very small. Apart from convention, the moral distinction between bullet and bacillus is by no means obvious : one may be more effective than the other, but their use seems equally justifiable or unjustifiable. The fact remains that to many doctors bacterial warfare is particularly repugnant for two reasons : it enlists against a human enemy the micro-organisms which are the foes of all mankind, and it diverts to destructive purposes knowledge which the profession has laboriously acquired in the hope of making people, of all nations, healthier and happier. We have reached a situation in which men of the highest character are prepared, from a sense of duty, to contemplate what they would normally regard as crimes of enormous magnitude. And this is precisely the state of mind we have so often condemned in our enemies.

Annotations

THE ASKWITH AGREEMENT ENDS

SINCE 1929 the terms of service and remuneration of doctors working for local authorities have been governed by the Askwith agreement made between representative organisations of the local authorities and the profession.[1] The Askwith scales were modified in March, 1946, and January, 1948 ; but plainly they need to be reviewed again in the light of the Spens reports on the remuneration of specialists and of general practitioners. Last July the B.M.A. proposed new scales [2] which would make the public-health service at least as attractive financially as other branches of the profession, and would thus reduce the danger that public health will cease to recruit and retain able young doctors. The Minister of Health suggested that these new proposals should be considered by the Medical Whitley Council, which he hoped would soon be set up : but the local-authority associations have not yet agreed to participate in the work of such a council. Their principal objection is that in each municipality the salary of the medical officer of health, and therefore of his juniors, has hitherto been closely related to that of the rest of the staff : there has been a sort of hierarchy in which all the chief officers—the M.O.H., the chief education officer, the architect, the treasurer, and others—receive similar salaries. The local-authority associations would be willing to join in Whitley Council negotiations on the salaries of their chief officers as a group ; but they have understandable misgivings about taking an active part in a Medical Whitley Council which may decide on higher pay for doctors and thus raise the question of increasing all salaries correspondingly from top to bottom of the hierarchy. The answer to these misgivings is, of course, that the hierarchical system must not be allowed to stand in the way of paying technical experts, such as doctors, sufficiently well to attract good men into a service where they are needed : not even the local authorities can get away from the law of supply and demand. But this answer has not yet convinced them, and they have not yet consented to enter the negotiations which are now so long overdue.

To expedite action, the B.M.A. in December indicated that it would apply pressure ; and on Jan. 12 it formally announced that unless negotiations opened by Feb. 28 the *British Medical Journal* would cease to publish advertisements of public-health appointments carrying remuneration below that of the association's draft scale. All must regret that so strong a step should be found necessary : it is a pity that coöperation between the lay and medical organisations should break down even temporarily, and for our own part we should have preferred to see the B.M.A.'s time limit extended a little, to give the local authorities a further chance of resolving their very real perplexities. However, with a considerable period of warning, the embargo has now been applied ; and this means that the Askwith agreement has in fact ceased to operate, and that fresh terms and conditions will sooner or later have to be negotiated. Application of the existing scales is no longer part of an agreed policy ; and we have therefore informed the parties to the previous agreement that we think it would be disadvantageous to the public-health service—and therefore eventually to the public—if our readers were invited to apply for appointments in the local-authority services before new negotiations begin.

1. The nine bodies represented in the agreement are the County Councils Association, the Association of Municipal Corporations, the Urban District Councils Association, the Rural District Councils Association, the London County Council, the Association of Education Committees, the Mental Hospitals Association, the Metropolitan Boroughs Standing Joint Committee, and the British Medical Association.
2. See *Lancet*, Jan. 29, p. 195.

Digitized by Google

RADIOLOGY OF CONGENITAL INTESTINAL OBSTRUCTION

CONGENITAL obstruction of the intestine is usually fatal. Babies stand operations well in the first two days of life, but obstruction is not usually diagnosed definitely at that time. In the first twenty-four hours infants need and take little, if any, fluid. After this period vomiting, abdominal distension, and failure to pass meconium may suggest that the bowel is obstructed; but (except in the case of imperforate anus) further time is likely to elapse before the diagnosis is certain enough to call for surgery, and by then the infant's condition is grave. In the early period it should be possible for radiography to convert suspicion into certainty. Barium is unnecessary and may be dangerous,[1] so it should not be given. The diagnosis rests on the interpretation of abdominal gas shadows. Middlemiss [2] has pointed out the advantages and pitfalls of the investigation, and shown how logical analysis of the picture enables one to locate the obstruction as well as diagnose it. He favours supine anteroposterior and erect posteroanterior projections. Ladd and Gross would add a lateral picture and one taken with the child inverted. Wasch and Marck [3] have described the normal distribution of alimentary gas on the first day of life—an essential preliminary to the diagnosis of abnormality. Air enters the stomach immediately after birth. Within an hour air-filled loops of small intestine may be identified in most infants. Between the first and third hours the ileum becomes filled and segments of colon appear. In three to eight hours air is seen in the sigmoid colon and rectum. In the eighth hour most of the abdomen is occupied by the small intestine. The amount of air in it decreases and by the twelfth hour the colon is prominent. This subject will repay study by obstetricians, pædiatricians, and surgeons, who may not always be able to get expert radiological advice at short notice.

VITAMIN A AND BONE GROWTH

EVEN before vitamins A and D had been distinguished from one another, it was observed that some dogs deprived of fat-soluble vitamin suffered from ataxia and incoördination of movement; but only recently has this disturbance been traced to disordered activity of osteoblasts and osteoclasts. In a lecture given at the University of Cambridge on Feb. 25, Sir Edward Mellanby, F.R.S., told how his researches led to this finding.

A necessary condition for the incoördination was shown to be a dietary deficiency of vitamin A. Careful observation revealed that the older the dog the less readily did the disease develop on an A-deficient diet. Some dogs become partially blind or deaf, or lose their sense of smell; and the ataxia is of a cerebellar type. Degeneration of nerve was found to be responsible; the vestibular, cochlear, and trigeminal nerves are particularly affected; efferent fibres are spared, except for a few from pons and cerebellum. Posterior root ganglia are also involved, and the degeneration of afferent fibres is greatest towards the upper end of the spinal cord; but there is no degeneration in the brain above the level of the red nucleus, although the retina may also be involved. Owing to the apparent similarity of the disease to convulsive ergotism, investigation proceeded for some time on the false assumption that the nerve degeneration was caused by a toxic substance normally counteracted by vitamin A. No success was achieved, but the curious selectivity of the "toxin" was remarked upon; for example, sometimes one side of the spinal cord was more affected than the other. Only when he came back to the problem after several years did Sir Edward make the key discovery which opened the way to the explanation.[1] The labyrinthine capsule of an affected dog was sectioned, and chunks of bone were seen to squeeze the cochlear nerve; thus the nerve was destroyed by compression and distortion of new periosteal bone. Corresponding bony changes were then observed elsewhere; for example, the cribriform plate showed a similar overgrowth of bone, destroying fibres of the olfactory nerve. In the skull the changes are greater in the posterior fossa, resulting in the compression and displacement of cerebellum and medulla with hydrocephalus and papilloedema; atlas and axis become grossly misshapen, with compression and distortion of the spinal cord.

The nerve degeneration is thus secondary to a disorder of bone growth. Epiphyseal and endochondral growth is relatively normal, but there is periosteal overgrowth of cancellous bone. This disorder is quite distinct from that seen in rickets, and calcification is normal. In sections of bone, however, osteoblasts and osteoclasts are found concentrated in abnormal positions, and there seems to be some reversal of their rôles. Small doses of vitamin A immediately restore their activity to normal,[2] and bony overgrowth is absorbed, although degeneration of nervous tissue may have advanced too far for restoration of its function. Thus in some way vitamin A controls bone growth in dogs; one factor directing the beautiful pattern of healthy development has been identified.

SOMATOTYPES

THE last few years have seen a renewal of interest in what is loosely called the constitution of the patient. This has happened partly because of the advances in endocrinology, genetics, and biochemistry which have made the background of human constitution far more understandable; partly, perhaps, because we are getting used to the triumphs of bacteriology and can see that there are places it cannot reach. Partly also, this revival is due to the activity of a few research-workers in this field, and the increasing clarity that they have brought about. Foremost among them is W. H. Sheldon,[3] whose system of classification of physique represents a great advance over any other in accuracy, flexibility, and comprehensiveness. Subsequent investigators are busy applying this technique of "somatotyping" in extraordinarily diverse fields, among them medicine and physiology, and in this issue Dr. J. M. Tanner, who has been associated with this work since 1943, describes the system and some of its applications.

Somatotyping has three phases—the taking of highly standardised and exactly posed photographs; the measurement of the photographs; and the assessment of the somatotype. Many who have not time to learn somatotyping, or even to measure photographs extensively, will wish to obtain photographs of their patients on which they can get an expert opinion, and with which they can contribute to research in the field. With this in mind, Dr. Tanner and Dr. Brian Stanford demonstrated on Thursday to the medical group of the Royal Photographic Society the photographic methods involved, and showed the first model of an adapted aircraft camera which will take up to 500 pictures without a change of film, merely by pressing a button. A commercial firm is now selling or hiring these instruments and will also process the film to exact specifications. So it is now possible for any hospital or practitioner to contribute

1. Ladd, W. E., Gross, R. E. Abdominal Surgery of Infancy and Childhood. Philadelphia and London, 1941; p. 28.
2. Middlemiss, J. H. *Arch. Dis. Childh.* 1948, **23**, 247.
3. Wasch, M. G., Marck, A. *J. Pediat.* 1948, **32**, 479.

1. Mellanby, E. *J. Physiol.* 1943, **101**, 408; *Proc. roy. Soc.* B. 1944, **132**, 28.
2. Mellanby, E. *J. Physiol.* 1947, **105**, 382.
3. Sheldon, W. H. The Varieties of Human Physique. New York, 1940.

Digitized by Google

with a minimum of effort to this field of knowledge and thereby hasten the accumulation of data on physique in relation to disease.

CHEWING THE CUD

SHORTLY before the war there was a Frenchman who earned his living by swallowing live frogs, up to eight at a time, and regurgitating them at intervals, to the admiration of his audience.[1] He prefaced his performance with liberal draughts of water, but apart from this there was no clue as to his technique. This was a dramatic illustration of the occasional occurrence in man of the bovine habit of rumination, mentioned by Aristotle and Galen under the names "merycasm" and "merycism," and, according to Long,[2] first described by Jerome Fabricius. Dambassis,[3] in recording 9 cases, divides the clinical picture into three stages. In the preruminative phase the patient eats hastily or inattentively, often drinking copiously at the same time. Left-sided abdominal discomfort and heaviness, with a sensation of fullness and distension, develop rapidly, and after about half an hour, at the peak of the discomfort, the phase of rumination appears. The patient eructates and involuntarily regurgitates into his mouth an undigested and still tasty bolus of food, which he chews and re-swallows. The process is repeated every two to five minutes for about an hour, with an increasing sense of relaxation. During the ensuing postruminative phase the subject returns to a normal state of comfort and well-being.

The origin of the condition includes a considerable variety of pathological states, such as short œsophagus, para-œsophageal hernia, pylorospasm (sometimes with the persistence of a conditioned reflex since childhood), aerophagia, cardiospasm, diaphragmatic spasm, carcinoma of the œsophagus, and various forms of imbecility. As might be expected, treatment is a matter of regularity and self-discipline in eating, together with the common-sense selection of suitable food and specific therapy for any known underlying abnormality.

THE INTERNATIONAL B.C.G. CAMPAIGN

THE evolution of the international B.C.G. campaign, since it was started by the Danish Red Cross in the spring of 1947, has lately been described by Ustvedt,[4] who has been appointed its technical director in Europe. Since last March the campaign has been conducted by the Danish Red Cross, the Swedish Red Cross, Norway's Aid to Europe, UNICEF, and the World Health Organisation, in coöperation with the governments, health authorities, and Red Cross organisations in the countries concerned. The chief objective is the tuberculin-testing of everyone up to the age of 18, and the B.C.G. vaccination of all the negative reactors. In Europe alone it is expected that some 40 million people will be tested and that about a third of them will be vaccinated with B.C.G. Hitherto more than 7 million have been tested, and at the present time $^1/_2$–1 million are being tested every month. The Moro plaster tuberculin test is the first to be applied to children under 12; children between 12 and 14 are tested with Moro plus Mantoux (0·1 mg. of tuberculin), and older youngsters with Mantoux alone (0·01 and 0·1 mg.); the dosage for a Mantoux test is not raised above 0·1 mg. for fear of provoking too many non-specific reactions. In principle only one technique is adopted in each country; so in the countries in which the Danish preference for the Mantoux test is endorsed, the Pirquet test (which is favoured in Norway) is not used; but it is expected that when the Norwegians provide the necessary staff for B.C.G. work in Bulgaria and Italy, the standard test there will be the Pirquet with adrenaline. The B.C.G. is given by intracutaneous injection; its effects are controlled by subsequent tuberculin-testing in only a few cases and by random sampling. As mentioned in our news columns last week, the mass of data obtained is to be analysed in Copenhagen by Dr. Carroll Palmer and his colleagues working with a grant from W.H.O.

1. *Lancet*, 1939, ii, 461.
2. Long, C. F. *Amer. J. med. Sci.* 1929, **178**, 814.
3. Dambassis, J. N. *Amer. Pract.* 1949, **3**, 309.
4. Ustvedt, H. J. *Tidsskri. norske Lægeforen.* Feb. 1, 1949.

A QUESTION OF COST

MOST minds are stirred by the mention of large sums of money; a hundred thousand pounds, if not within our ken, is still not beyond our imagining. But when the talk shifts into millions, imagination baulks; the ordinary man's experience sets up no landmark in the sea of high finance. Thus the news that the anticipated cost of the National Health Service in Great Britain in the next fiscal year is £259,727,600 [1] is unlikely to cause much stir except perhaps among those responsible for administering the country's affairs. The significance of this figure is perhaps more readily grasped in personal terms: it means that the cost will be some £5 15*s*. per head of population. It means also a slight advance on the per-diem cost of operating the service in the first nine months; the total of which is reckoned at about £208 million,[2] including £19 million of non-recurring expenses in the form of liabilities transferred to the Government.

In the coming year there is to be a tighter grasp at the centre on expenditure; and the Minister of Health has already asked hospital authorities to reduce their estimates by £9$^1/_4$ million. He urges that expenditure affecting the wellbeing of patients should not be curtailed; but some capital works which would otherwise have been put in hand will be postponed. The *Daily Telegraph* (March 1) reports Mr. T. Knox-Shaw, chairman of the board of governors of Cambridge United Hospitals, as saying: "The only way we can carry out the instructions is by reducing staff and closing wards." For these Cambridge hospitals, expenditure is to be reduced from a proposed £451,000 to £425,000, even though the larger estimate did not include increased payments from the application of the Spens report on specialists' pay, entailing a further £48,000. The Ministry of Health is reported to have said that this increment will have to be met out of the sum now allowed.

NO ROOM AT THE HOSPITAL

THE rising pressure on London's hospitals is reflected in the parallel growth of the demands on the Emergency Bed Service. Early in February the service was receiving each day some 185 applications for admission, of which 50 could not be met. Undoubtedly some at least of these 50 patients were in real need of hospital treatment; and it is unlikely that where the E.B.S. had failed in securing immediate admission, any other agency would succeed. Dissatisfaction has been expressed in the gravest terms by the local medical committee for London, which is especially perturbed by the delay in admission of patients with acute-on-chronic disorders; the committee is concerned by reports of "many patients who have died but whose lives might have been saved" if energetic action had been taken to secure prompt attention. There is no hint that serious illness is more prevalent now than a year ago, but there is every indication that more patients are being referred for admission. In the long run the agreed solution is to use hospital beds more economically and to bring greater numbers into use. But the need of short-term expedients is daily more evident. On Dec. 18 we discussed some of the possibilities. Another is that the London hospitals perhaps increase the proportion of beds allotted to emergencies, deferring admissions which, though desirable, are not vital.

1. 1949–50: Vote on Account. Civil Estimates: Estimates for Revenue Departments and Estimate for the Ministry of Defence. H.M. Stationery Office. Pp. 8. 2*d*.
2. See *Lancet*, Feb. 19, p. 312.

Digitized by Google

Special Articles

SOMATOTYPES AND MEDICINE

J. M. TANNER
M.B., D.P.M. Lond., M.D. Penna.
From the Sherrington School of Physiology, St. Thomas's Hospital

IT was the practice of the early physicians to look carefully at their patients and consider at length what manner of men they were. Both in Ancient Greece and in India the observations were acute enough for some generalisations to be made and accepted. Thus men suffering from certain diseases, it was said, differed in appearance from the general run; and men with one disease often differed from those with another. Phthisis, the wasting disease, most commonly attacked those who had from birth been thin, spare, and slender; whereas apoplexy was a disease of the broad-shouldered, thickset, and rotund. There were other differences, of course, besides the physical ones. Likewise there were exceptions to the rule. But in time physicians came to regard people as approaching one of two types—the *habitus phthisicus* or the *habitus apoplecticus*. And they believed they could make some crude prognosis of disease from this classification.

It is humiliating that, at least until a few years ago, we ourselves could do no better. Probably this is the only branch of medicine that has not advanced substantially in the last two thousand years. Yet the promise is plainly there, as will be seen from the fragmentary data discussed later, and we have the tools now to test our generalisations and to make far finer discriminations than the ancients, if we choose to try.

On qualification, the average doctor of today knows less of these matters than his Hippocratic colleague. Probably he has never heard of the phthisic and apoplectic types, though he may have been told that a psychiatrist called Kretschmer divides people into three large groups—pyknics, athletics, and leptosomes. Of the greatly superior system of Di Giovanni, Viola, and the Italian school he will know nothing. He will be able to recognise many pathological types of liver and spleen, but he would be astonished if asked to argue from the shape of spleen or liver the shape of the man himself, as could the pathologist Beneke. Rumours of heart shapes will have reached him, but certainly no exact statements; and he will have heard something about a difference in physique between sufferers from peptic-ulcer and from gall-bladder disorders—the lone persistence of George Draper in America over some thirty years has not gone entirely unrewarded.

But there is more in the subject than these vague whisperings, both as a discipline and as a medical aid, and recently interest in it has again become widespread. There are many reasons for this. The brilliant flames lit by Pasteur and Ehrlich have been brightened rather than dimmed by their successors; but our eyes are becoming accustomed to them, and we are beginning to see beyond to the dark places they cannot reach. Biochemistry, endocrinology, genetics, and statistics have been our chief guides into the shadow. (A formidable quorum, you may say, but no more intrinsically formidable to the modern medical student than were the culture medium and the carving knife to his predecessor.) Diabetes is an obvious example of this process. From the other side, internal medicine and psychiatry have contributed to the interest, chiefly by laying emphasis once more on the patient as a whole living organism, functioning as a whole and getting sick as a whole. The specialist on the pineal body again finds it expedient to know something of the neighbouring structures. And so the patient once more gets looked at; and this time the physician, trained in quantitation, wants to say something more accurate about what he sees than habitus apoplecticus, or an athletic type.

SHELDON'S SOMATOTYPE SYSTEM

There have been several more or less recent systems of classification which provide, or claim to provide, this more accurate assessment. The method devised by W. H. Sheldon[1] is much the most flexible, accurate, and comprehensive. Indeed, it has only one rival, which may ultimately overtake it but at present is far less practically useful—the factor analysis method.[2] Sheldon's system renders Kretschmer's classification obsolete, because it has all the latter's advantages and only some of its disadvantages. Moreover, Kretschmer divided mankind into three disparate *types*, and thereby made a cardinal and ineradicable error. He assumed that there was a trimodal distribution of body-build among people, with large numbers belonging to each of his types and only a relatively few mixtures. He failed to grasp the idea of continuously varying *components* of body-build, each distributed smoothly and unimodally in the population. Sheldon began from the premise of continuous components; he writes:

> "The concept of types has been useful in the study of personality, but, like the poles supporting a clothes-line, it provides only end suspensions for distributive classifications. As the line becomes filled, the notion of types recedes and finally vanishes altogether, perhaps submerged under a smooth distribution. The path of progress is from the notion of dichotomies to the concept of variation along dimensional axes." [1]

Sheldon began by taking large numbers of nude standardised photographs of college students, showing front, side, and back views. After a time, he had pictures of 4000, which he could look at carefully and at leisure. He sorted them repeatedly, trying to pick out extremes. Disregarding simple size, he found three extremes of body-build, each of which, he argued, represented the end man in the distribution of a component of build present to *some* extent in every member of the 4000. Having thus systematised his material into the product of three components, he next assigned to each individual a score in each component, by using a rating scale with 1 as a minimum and 7 as a maximum, the intervals being defined as equal-appearing—that is, the difference between a score of 1 and 2 appeared to the rater to be equal to the difference between 2 and 3, and so on. Thus finally, the first extreme example was rated as a 7–1–1, the maximum in the first component and the minimum in the second and third; the second extreme was a 1–7–1, and the third extreme a 1–1–7. The three components were called endomorphy, mesomorphy, and ectomorphy.

Fig. 1 shows three men fairly near the extremes. The man high in endomorphy and low in the other two (A) approaches as near the spherical as nature permits: he has a round head, a short neck, a large fat abdomen which predominates over his weak thorax, and weak floppy penguin-like arms and legs, with "hamming" of the upper arms and thighs. He has an extensive deposit of subcutaneous fat, and, at any rate when young and well fed, is a natural recipient of the adjective pneumatic. The 1–7–1, the extreme in mesomorphy (B), is a very different creature. This is the Herculean man; a cubical head, muscular neck, broad and muscled chest dominating an abdomen where the outlines of the abdominal muscles are clearly visible even in repose. The arms and legs are thick, right down to the wrists and ankles, strong and heavily muscled, and the subcutaneous panniculus is entirely lacking. The 1–1–7 (C) differs entirely from both these two. This extreme in ectomorphy has a thin peaked face with a receding chin and a high forehead, a thin narrow chest and drooping shoulders, little muscular outlining and no sub-

1. Sheldon, W. H. Varieties of Human Physique. New York, 1940.
2. For bibliography of this system, and a discussion of its relations with Sheldon's classification, see Tanner, J. M. *Proc. R. Soc. Med.* 1947, **40**, 301.

Digitized by Google

cutaneous fat. His arms and legs are spindly, his costal angle acute. His whole body is narrow, particularly anteroposteriorly. Turn a 1–1–7 sideways in a bad light and he is gone.

Naturally, only a very small proportion of people look like this; the majority have a moderate amount of each component, and so have as their "somatotype," as the set of three ratings is called, such numbers as 433, 344, or 352. In fig. 2 are illustrated three physiques more common than those in fig. 1. These three also show the same general dominances, D being higher in endomorphy than in the other two components, E higher in mesomorphy, and F in ectomorphy. It takes rather more care to see the distinctions this time. The differences between D and E, who are fairly evenly matched in ectomorphy, will be found to grow greater and greater the longer the two pictures are compared point by point. This is a difference of endomorphic and mesomorphic endowments.

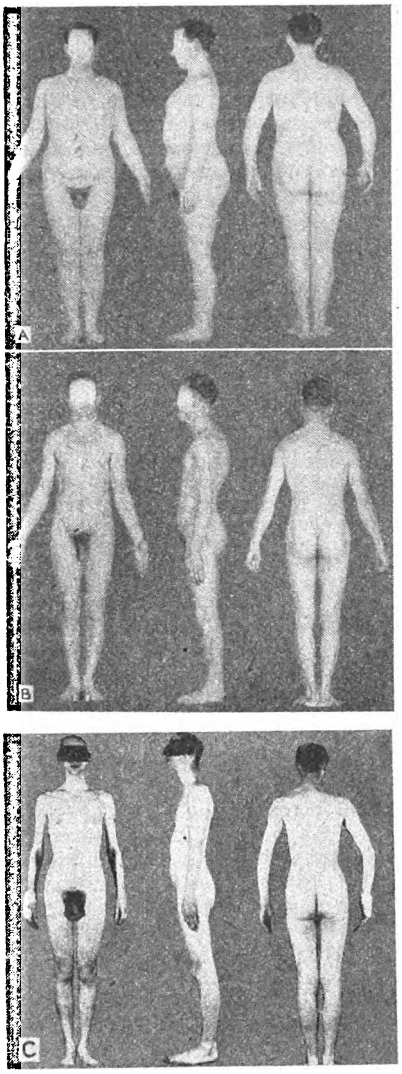


Fig. 1.

The three components are not independent of each other; they are negatively correlated, so a high rating in one precludes to some extent high ratings in the others. Thus 771s and 555s do not exist, but 641s and 444s do. In Sheldon's 4000 pictures there were 76 somatotypes, but only about 50 of these were at all common. But the number of somatotypes is really quite arbitrary; the point is that the somatotype is not like the old fixed type at all; it merely results from making artificial discontinuities in three continuous scales. It is a pigeon-hole into which is placed everybody who, on the continuous scales, is nearer that pigeon-hole than any other. In fact, most workers in the field now use halves on the rating scale, converting it to a thirteen-point scale, with a correspondingly larger number of smaller pigeon-holes.

That is the main outline of Sheldon's extensive system. There are other ramifications, chief among them being methods for estimating the femininity of a male physique, and the *dysplasia*, or variation in somatotype from one region of the body to another. It is impossible to do justice to this brilliant work in a short article.

RESULTS SO FAR

Already, largely through the efforts of C. W. Dupertuis, somatotyping has begun to contribute to medicine. Perhaps the most striking and interesting result is in diabetes mellitus.[3] Dupertuis, a physical anthropologist, noticed that diabetics fell chiefly into two distinct morphological groups. In male diabetics, those of group I, besides being somewhat larger than group II, had an average somatotype of about 532½, whereas group II had an average of about 343, with a wider spread than group I. His clinical colleagues, on being told this, classified independently and from the history alone some 225 patients as either pituitary, insulin-insensitive, or pancreatic, insulin-sensitive, diabetics. The coincidence of morphological and clinical groupings was 88%, pituitary diabetics being the group I patients.

Dupertuis notes in his book that peptic-ulcer patients and gall-bladder patients differ on the average, but the spread of the ulcer group is very considerable. The average male somatotypes were 34½3 and 442½. There are also differences in somatotypes between patients with rheumatoid arthritis and with osteoarthritis, a hint of two groups in thyrotoxicosis, and some very suggestive but as yet unpublished figures on various cancer groups.

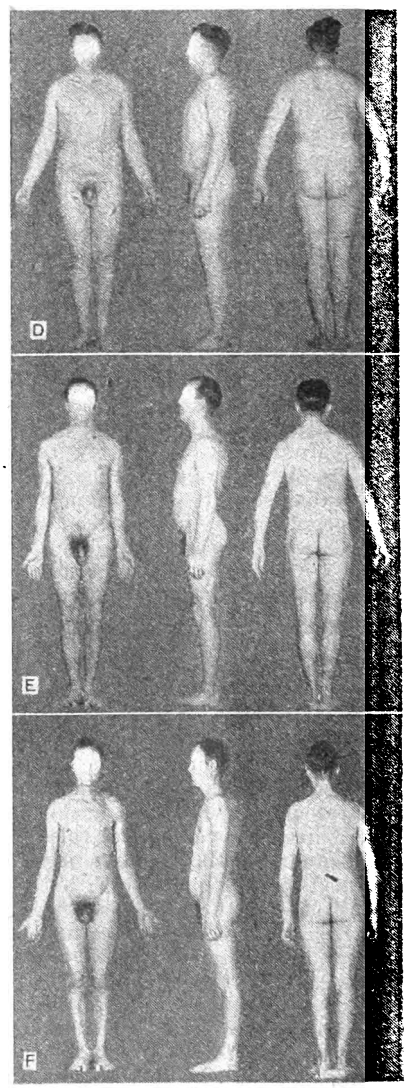


Fig. 2.

As for the fundamental relations between physique and physiological function in the normal person, little has as yet been done. I have ventured a very little way into the fringe of this enormous and unsurveyed field. There seems to be a relation (of which evidence existed before the present studies) between the serum cholesterol level and the physique, in this instance endomorphy. For every rise of 1 in endomorphy rating there is an average rise of 11 mg. per 100 ml. in the serum-cholesterol level.[4] This may partly explain why endomorphic people are most liable to get gallstones. Certainly the observation is connected with the fact that in pregnancy both cholesterol and subcutaneous fat increase. And certainly behind it lies endocrine secretion as the immediate cause. Body temperature seems also to be related to physique, but some other functions, notably heart-rate,

3. Draper, G., Dupertuis, C. W., Caughey, J. L. Human Constitution in Clinical Medicine. New York, 1944.
4. Tanner, J. M. *J. Physiol., Proc. physiol. Soc.* (in the press).

Digitized by Google

cardiac output, and probably blood-pressure, are independent.[5]

The usefulness of studies of physique in the prevention of disease and in the furtherance of student and school health programmes is being investigated, on Oxford undergraduates, in conjunction with Dr. R. W. Parnell of the Nuffield Institute of Social Medicine.

In psychiatry there are clear differences between the various groups of psychotics [6] and also, it seems, between neurotics and normals.[7] And in the study of normal psychology there is ever-increasing evidence of links between physique and various traits of behaviour, including written masculinity-femininity tests,[8] selection of careers,[9] and the deeper levels of temperament.[10]

TECHNIQUE AND PRACTICABILITY

The field, both in normal physiology and endocrinology, and in clinical medicine, is wide open. It seems at first sight that any hospital outpatient department, or any practitioner for that matter, could at least contribute valuable material, or better, make his own investigations. How far is this practicable? Many may feel an initial enthusiasm, only to be damped by difficulties in achieving their aims. Is this activity possible for any but the largest research institutions?

The answer is in the affirmative, with a few provisos. For obtaining suitable pictures all that is necessary is a little care, a little money, and a day's training. Measurements as well as ratings must be obtained, for reasons given later. The camera must be a long way from the subject, to avoid errors in measurement arising from one part of the body being sensibly closer than another. I prefer a 10 metre (about 30 foot) lens-heel distance. A turntable to turn the patient is needed and preferably a camera which takes many pictures without a change of film. My colleagues and I devised a technique for use with a Leica camera and the Hektar 13·5 cm. lens when dealing with hospital patients,[11] and we later carried out extensive tests to see how accurately measurements could be made from the enlargements of these pictures.[12] Dr. Brian Stanford has devised a better apparatus which overcomes the difficulties caused by the smallness of the Leica image. This is a converted aircraft camera, and with it the doctor can take large numbers of pictures by merely pressing a button. A commercial firm now makes, sells, and hires such cameras, and will process the film as well, supplying the casettes and returning the finished enlargements. With this step the photographic problem seems to be solved. However, the study referred to above demonstrated that the chief error arises from difficulties in posing. This must be done very carefully and in a particular way (which now differs somewhat from the poses illustrated in the figures). Hence the necessity of a day's tuition on the part of the doctor, nurse, radiologist, or photographer who is to take the pictures.

Getting the pictures presents no great difficulty. How about somatotyping them? Sheldon has provided tables of measurements which automatically give the investigator the correct somatotype over the age range 16–20 years inclusive. Seventeen measurements must be taken, and direct-reading compasses devised for doing this [12] are now obtainable. Outside this age range yet only subjective ratings are possible. Actual somatotyping is not a difficult technique to learn. experts can routinely get almost perfect agreement with measurement results. But in view of this subjectivity somatotyping without the tables should not be attempted without a proper preliminary training in the method.

If the investigator has no intention of becoming a skilled somatotyper, he can still measure his pictures; somatotyping is not the only way of characterising physique and there is in any case a great need for large series of measurements and modern statistical control both of somatotypes and other physique procedures. And even for those without time or inclination to measure, there is the material to be collected. The stage is set for all those who concern themselves, from their several points of view, with the question "Who, in terms of morphology, gets what?"

SUMMARY

In "somatotyping," the system of describing body-build developed by Sheldon, three basic components of build are postulated, and everyone has some of each component. There are no disparate "types," only scores in each component of from 1 to a maximum of 7. Roughly speaking, the first component connotes fatness and sphericity, the second muscularity, and the third slenderness and linearity. The somatotype of a person is his score in each of these components—for example, 3–5–2 or 1–4–5.

Attention is drawn to the medical usefulness of studying patients' physiques, and the example set by Dupertuis in differentiating pituitary and pancreatic diabetics is instanced. The technique is discussed from the point of view of an outpatient department or doctor who might wish to institute such a study. Standardised pictures, from which accurate measurements can be obtained, are necessary, and the photographic procedure for getting them is discussed; it is now possible to hire or buy suitable cameras and have the photographs processed commercially. Somatotyping over the age range 16–20 years can be immediately embarked on by anybody with such pictures, though outside this range some training in procedure is necessary, owing to the lack of anthropometric tables.

5. Tanner, J. M. *Amer. J. med. Sci.* 1944, **207**, 684; *J. clin.* (in the press).
6. Moore, T. V., Hsu, E. H. *Human Biol.* 1940, **18**, 135. *Ibid.* 1942, **14**, 21.
7. Rees, W. L. *J. ment. Sci.* 1945, **91**, 89.
8. Child, I. L., Sheldon, W. H. *Character and Personality* **10**, 23.
9. Seltzer, C. C. *Amer. J. phys. Anthropol.* N.S. 1945, [illegible]
10. Sheldon, W. H. Varieties of Temperament. New
11. Tanner, J. M., Jones, M. *J. Neurol. Neurosurg. Psy* **11**, 61.
12. Tanner, J. M., Weiner, J. S. *Amer. J. phys. A* 1949, **7**, no. 2.

ACADEMIC SALARIES

THE Chancellor of the Exchequer states that the University Grants Committee has written to vice-chancellors indicating revised general limits of salaries in medical and dental schools for which it would be prepared to make supplementary grants. The revised rates for full-time posts are:

Clinical Posts (to operate not earlier than April 1).—Professors, £2250–2750 a year; lecturers, £600 to maxima of £1500–2 [illegible] a year (or in cases of special responsibility, £2500).

Preclinical Posts (to operate not earlier than October 1).—Profes[illegible] £2 [illegible]–2500 a year; lecturers, £600 to maxima of £1200.

In [illegible] ...s of *readers* are to be within the range of the ma[illegible] ...ed for lecturers.

The [illegible] Grants Committee are leaving the univer[illegible] ...es in borderline cases which posts are cli[illegible] ... But they think it reasonable that certai[illegible] ...ments of pathology and bacteriology shou[illegible] ...ld.

... Committee and the Committee ... Pensions were relevant to ... with the Government's ... on they came to the ... recommendation of con... ...ended by the Spens ... of the salaries of ...sities, otherwise the ... these schools might

... vice-chancellors ... on ... ments is still being

Digitized by Google

The Wider World

NUTRITION AND HEALTH OF CHILDREN IN FIVE COUNTRIES OF SOUTH AMERICA

R. PASSMORE
M.A., D.M. Oxfd, F.R.S.E.
Of the Department of Public Health and Social Medicine, Edinburgh

4. Peru

THE flag of Peru flies over three distinct countries—the Orient, the Sierra, and the Coast. Each has different and independent economic, agricultural, and social problems.

THE ORIENT

The Orient, covering some 550,000 sq. km. of forest and jungle in the great Amazon basin, is separated from the capital, Lima, by the great mountain mass of the Andes. It is one of the most thinly inhabited regions of the world, and many of its people (who are reported to number only 370,000) are primitive jungle-dwellers. Iquitos, the chief city, is an Amazon port and naturally looks to the east rather than to Lima for future developments. Although the Orient represents 44% of the total area of Peru, it contributes only 2% of the cultivated land.

The principal crops are said to be potatoes, mandioca, maize, vegetables, and fruits (bananas); little or no milk is available to most families, but river fish are sometimes plentiful. In limited surveys Señorita Alicia Roncal found that many families were short of food and the children frequently undernourished. Figures for Iquitos support the view that something approaching half the deaths are in children under five years of age.

The Orient may be described as a vast undeveloped jungle, often inundated by floods, and sparsely populated by a people ignorant of hygiene and mostly without medical aid.

THE SIERRA

This is the great mountain region of the Andes. Its inhabitants, numbering probably at least 3 million, are simple agriculturists of Indian stock dwelling at 7000–14,000 feet—the majority around the 11,000 mark. Flying from Cuzco to Lima one can appreciate the extraordinary isolation of these people. The inhabitants of a small village are usually separated by huge mountains from their nearest neighbours in the next valley. Each community must be and must remain an independent self-supporting human society. The possibilities for road-making are very limited. As mountain ridge succeeded valley, one was filled with admiration for the genius of Pizarro, which enabled him to bring his small army across this hostile country to the Inca capital.

Most of those Peruvians who think and write about the living conditions of the Indians are appalled at their apparent poverty. The mean squalor of their homes, the absence of any hygienic laws or appliances, the lack of any of the amenities or comforts of our age, the absence of any medical care for the sick and injured—all these are obvious. On the other hand one or two of my informants pointed out that the Indians also lacked most of the social ailments of our industrial and urban age. From their own land they were able (except when disturbed by floods and earthquakes) to grow a sufficiency of simple foods. Their flocks provided them with wool from which the women made such cloth as was needed, often with bright and elegant designs. Within their small communities it was possible to achieve social security and a happiness unknown to us.

My own impressions lead me to support this minority opinion that the Indians are not so badly off. At the railway stations between Puno and Cuzco the platforms were filled with sturdy urchins, who had a vigour and even swagger about them. The large Cuzco bazaar is the dirtiest that I ever saw: yet it was full of grains, fruits, vegetables, meats, and home-spun cloth; in fact all the primitive essentials of life (except perhaps soap) were being purchased by even the poorest. The children that I saw did not look underfed. The city has a surprisingly good hospital with a children's ward of about 30 beds. On my arrival the patients got up, rushed out of doors, dragging their splints and plasters, and insisted on a photograph. They were eager active kids. The only case of malnutrition was in a visitor up from the coast with chronic malaria. Not surprisingly, the infectious block contained 20 cases of typhus.

The history of the city of Cuzco is relevant to the modern social problems. The huge ruins of the temples, palaces, and fortresses of the theocratic Inca régime provide abundant proof of the possibility of an ordered centralised government among the peoples of the Sierra. These magnificent examples of the stone-mason's skill could only have been set up by a large and powerful social organisation. After the defeat of the Incas, the conquistadores filled Cuzco with splendid examples of the best products of the art of the Renaissance. Churches, private palaces, pictures and wood carvings, and the works of the finest schools of European architects, painters, and craftsmen, abound in Cuzco. They provide evidence of a virile active civilisation existing 200–300 years ago. Today the churches are in disrepair and dirty, the fine houses derelict slums, the pictures covered in dust and dirt, the carvings uncared for and damaged. Modern Cuzco is utterly decadent. Having seen in Asia and Africa the fine work of so many Churches in setting up schools, running hospitals and dispensaries, and caring for orphans and widows, I had looked forward to seeing similar humanitarian work in South America; but I found none. Direct questions to medical men invariably brought the answer that the Church in no way helped with their fundamental social problems. This is, I believe, an important factor determining the wretched condition of so many children.

The chief crops of the Sierra are potatoes, maize, fruit, barley, wheat, and vegetables. Sheep, goats, cattle, and llamas provide wool, some meats, and a little milk. These are the basic needs. Whether the food-supply is sufficient must be a matter of personal impression. Señorita Roncal has carried out studies in Cuzco and neighbouring villages and found many families living on a bare subsistence. During my visit I could see no evidence of serious underfeeding. But the high mortality-rates in children again reflect the primitive conditions of living, even in the towns. In 1946 infant mortality was estimated at 197 in Cuzco and 184 in Puno.

The Indians in Peru, as in Bolivia, are all coca addicts. Children start to chew the leaves at an early age. As in Bolivia, there is an extraordinary difference of opinion on the effects of addiction.

THE COAST

This is a narrow belt lying between the Andes and the Pacific. It is never more than 60 km. wide, but the length is 1800 km. There is rarely, if ever, any rain. A natural desert is broken up by areas of cultivation where small rivers run through on their way from mountain to ocean. These are used as sources of irrigation, and in the irrigated areas abundant crops of rice, maize, sugar-cane, and cotton are grown. There are also rich vegetable gardens and orchards and a few fine dairy herds. Thus, the economy of the Coast closely

Digitized by Google

resembles that of Egypt, the mighty Nile being replaced by 20 or more small rivers. The city of Lima dominates the Coast. Like Cairo it is beautiful; there are fine boulevards, noble buildings, luxurious clubs, and gorgeous flowers. As in Cairo, there are also ugly slums and plenty of tuberculosis and syphilis. Both cities are concerned with the world cotton market. Before the war cotton formed 27% of all Peru's exports.

In the three principal towns of the Coast, in 1946, the proportion of deaths occurring before the age of five ranged from 30 to 38%. I saw many children from the poorer districts, and it would be idle to pretend that they were well nourished: many looked small and lethargic and lacked energy. Yet they were all a long way from starvation, and in far better condition than millions of Asiatic children. I only saw two cases of deficiency disease, both in a large children's hospital.

Venereal diseases are probably slowly being controlled; but 6·2% of the women attending the antenatal clinic in the Rimac district in 1947 gave positive serological reactions for syphilis. How small a part organised religion plays in stabilising the home is shown by the fact that 48% of births registered in Lima in 1946 were illegitimate.

Lima is expanding rapidly. The birth-rate is high and immigrants are coming in from the countryside to work in new industries. But the population seems to have already outgrown its food-supply, its housing, and its sanitary systems.

CHILDREN'S HEALTH SERVICES

A special department within the department of public health is concerned with both preventive and curative medical services for mothers and for children up to five years of age. Its work is based on the following institutions:

Centres for Mothers and Infants—In 1948 there were 50 of these in the whole republic (18 in Lima). In 1946 about 68,000 children under five attended these centres—i.e., about 6% of the estimated population of that age. The antenatal clinics were attended by about 13% of all pregnant women in the capital. Also, home visits are organised by the centres.

Child-guidance Clinics now number 3 (2 in Lima).

Day Nurseries.—There are 15 in Peru (8 in Lima).

Hospital Services.—A large well-equipped hospital for children in Lima has 500 beds and a nurses' training school. There are children's and maternity wards in the provincial hospitals; in all of these together there are 1200 maternity beds and 900 beds for children.

School Refectories.—Peru has 240 of these. All meals are free, and about 17,000 children receive them—i.e., 1·2% of the estimated population of school age.

Popular Restaurants.—In 1947, popular restaurants and dining-rooms served 3,337,817 free meals to children and pregnant women and 471,144 to students; also 2,471,144 meals to workers on payment.

On the whole, these children's services are well planned. Many of the staff were clearly well trained and very enthusiastic. However the scope of the services is pitiably small, even in the towns.

Shortcomings were invariably attributed to lack of money. To sit in the lounge of a luxury hotel in Lima, surrounded by wealth, and to be told that nothing can be done for lack of money was, I found, somewhat irritating. Peru's urgent need at the moment is for more taxes. Until there is evidence that the country has managed to gather in some of the surplus wealth of her rich citizens, Peru can hardly have a claim on international funds for financial aid with her social services. The most urgent task of the many fine workers engaged in social work throughout the country is to create an enlightened public opinion.

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN I was a student I thought of diabetes as a rather mystical disease mainly concerned with the formation of peculiar fatty acids with long names. When I had to run a diabetic clinic on my own I saw diabetes in the raw and found what an intensely practical complaint it is. In the first place, this business of hyper- and hypoglycæmia. When the clinic began after breakfast blood-sugars were high and the waiting mob on the benches was as complacent and easily manageable as a collection of Labour M.P.s. Towards lunch-time, as the clinic ran late, the P.Z.I. took over and an angry hum rose from outside the ever-opening door. They began insulting the nurses, arguing with each other, and coming in full of truculence with little beads of sweat on their brow.

The question of how much insulin the patient was actually taking caused me a great amount of confusion and multiplication with the double and quadruple strengths. Asked point-blank the daily dosage, the disquieting reply was often, "Dunno, doctor, Mrs. 'Arris gives it me." Or, more terrifying, "A syringeful." As for diet—"Now, missus, are you on a diet?" A dog-eared Lawrence's card is produced from the handbag. "Oh yus, doctor, bin on a diet for years. Always 'ave this on the dresser." "Well, how many portions are you on?" Blank astonishment and reproach for unfair questioning. "It says in your notes here, missus, you're on 12 portions. Is that right?" "That's it doctor! Twelve points!" "And do you understand what 12 points means?" Another confounded silence, the eye hopefully scanning the diet card. Eventually it comes to rest on the "Unlimited Vegetables" section. Then, triumphantly and almost invariably, "Oh yus, doctor, I always eats plenty of *greens*."

I know there are thousands of intelligent diabetics who live well-regulated and normal lives, but sometimes towards the end of the morning I begin to wonder whether Banting and Best did not, after all, live in vain. Perhaps that is because by then my own blood-sugar is beginning to get pretty low.

* * *

In June it became manifest that every kind of patient, regardless of income, social standing, distance from my house, nosophobic or iatrophilic disposition, would present a white card and thereafter believe they had squared all possible accounts. Some thought it a legal duty; many supposed no hospital service would be open to them save through the "panel doctor"; others wanted their money's worth and fancied, as they still do, that their whole weekly contribution would fall straight into the doctor's pocket. No-one in authority attempted to disabuse them, just as no-one, to this day, has thought well to explain to the citizen that the doctor cannot order him two pints of milk a day and a few eggs if he thinks it would do him good.

So they offered their white cards and made it clear that, short of playing the oranges-and-lemons arch, a part for which I lack both will and cunning, I must be either whole-time "panel" or whole-time private practitioner. Given such a health centre as may in ten or fifteen years exist, the first might have seemed a just tolerable, a not impossible choice; but a calculation within even my mathematical capacity, based on experience of the demands of my own little panel of 300, proved that even 1000 such patients, if they and I treated each other as aforetime, would disrupt the foundations alike of my personal and my professional life. Down would come baby, cradle and all. Among the rubble of my household the heavy rescue party might dig out whatever my patients, "using the New Service to the full," would leave of my medical soul.

So I attempted no financial calculation or estimate but stayed out, perforce abandoning my "panel."

The result, in a sense, is good. I am by no means unemployed; I can neither be exploited by my patients nor regulated by the Minister; I have time to do my

Digitized by Google

work as I believe it should be done, and I have powerful incentives to do it well. Not only am I paid and thanked directly for it, but, if I am now to make good, the service I give must be so much better than that which the State provides as to be worth both my fee and the cost of the medicines I order. Here is the spur of competition at its sharpest. My native laziness hardly dare show her head.

One might think the competition *too* sharp, the weights I must carry too heavy. I give no marks, either for sense or justice, to those responsible for the handicapping, but they have so loaded their own horse that my chances are better than they look at first glance. In plain language, until the N.H.S. can offer the citizen with, let us say, recurrent abdominal pain 30–45 minutes of his doctor's undivided attention for history-taking, examination, and discussion, 20 minutes for mere discussion of some human domestic problem, available by appointment with reasonable punctuality, or 15 minutes at the bedside if the case requires it, I shall not lack work; and until taxation eliminates the detestable bourgeoisie my patients will gladly pay me.

So far so good. I am practising the Art, and, in so doing, am playing my small part in keeping the Art alive. For it cannot survive, even as much as music and painting could and have, through its stored records. If not practised it must die.

But here comes in the folly of the thing. Before July 5 I could and did serve, according to my lights, quite a wide range of "income levels." The dwellers in Council flats, in the attics of unattractive houses, or in some unfashionable mews formed a fair proportion of my practice and were by no means the least liked or the least grateful of my patients. They are gone. I can serve them no longer. Quite against my inclination and intention I have become the doctor of a limited social class, not a rich or idle class—on any sane view many of them are the best of citizens—but a class distinct from wage-earners and the poor.

I feel that a ham-like hand, directed by an ill-informed and unperceptive mind—alas, a collective, not an individual mind—has thrown a sabot through my practice, seeing but not comprehending the target. Odd (in passing) that the sport of throwing wooden shoes, almost by definition a revolutionist's pastime, should be ascribed so commonly to the victims of revolution who go more lightly and more flexibly shod. Poor chaps! They have no sabots to throw.

How fascinating are the ethics of this non-coöperation! To Mr. Bevan and to some of my former Leftish patients—but not, curiously enough, to some of the Leftest—I am, by staying outside the N.H.S., trying to wreck it. Mr. Bevan, I fear, wants to liquidate me; leaders of the S.M.A. unquestionably do, and some quite devoted former patients would regard themselves as traitors to the cause if they consulted me now. Viewed by the eye of the God of Good Citizenship or even by the perfect witness of all-judging Joy, how do I stand? I cannot tell. I can but [illegible] as far as a man may and take a look.

Of course, if the exal[illegible]lly and the making low of every mo[illegible]gnificent of the crooked and the [illegible] *summum bonum* there is no more [illegible]y practice something of a hillock. [illegible] quality of service given is as o[illegible]rodsheder and my only hope o[illegible]rose on preserving whatever [illegible]ves of surface I may possess. [illegible]ved, is, again, the very [illegible]hance. I would not attempt [illegible]o and [illegible] to be [illegible] pity [illegible]ndscape. [illegible]g. if [illegible] through [illegible] *malum* spiritual [illegible]by unless [illegible] poverty? [illegible] because [illegible] now [illegible], [illegible]? I [illegible] [illegible] lio[illegible] good [illegible] pro[illegible] [illegible] fell [illegible]

to supply for the citizen what at present I think the Service dare not claim to give—unhurried examination and discussion, alike in sickness and in health. While for the Service itself I (meaning I and all others like me) supply that pace-maker and competitor which only a fool and an idler is not glad to have. Note also that we relieve our struggling Service colleagues of some exacting and critical patients and the taxpayer of a fraction of the drug bill, and it is almost inconceivable that a Service in its senses should wish to discourage us or to diminish our numbers. In sober earnest I believe that a country which knew its own good would resolutely encourage us as a permanently necessary adjunct and support of even a full-grown State service. The Service may fail; but not for lack of our presence within it or because of our existence outside it.

The accusation that I am failing to do my share in carrying the collective burden of the profession strikes more nearly home. What can I say? Only this: that in my judgment to undertake responsibility for 3000 or even 2000 unselected local inhabitants would involve for me, a slow worker, the abnegation of medicine. I could, I suppose, have signed on, accepted the first 1500 that came; refused more and supplied the goods to those. If such a vow of poverty complete with hair shirt was indeed my duty I admit I have failed. I was not and am not saint enough. My motives are as mixed as motives always are. My profit or loss in £ *s. d.* can never be known. The end is not yet; but that goes for the State too. Generations to come may yet bless those who preserved the tradition of independent medicine. There was a restoration in this country once before.

* * *

It is not often that one has the opportunity of witnessing the results of a social revolution which one has done something, however little, to bring about. Yet there were two consultants and a retired Colonial judge, in the ecclesiastical surroundings of Church House, still echoing with the memories of a much more publicised tribunal, sitting to hear the first appeals from a medical board under the new National Insurance Act. The first appellant had let a wooden girder fall on his knee six months ago. Though the medical board had found that, in the quaint legal language of the Act, he had suffered no loss of faculty, he disagreed with them. His appeal was dismissed.

The second appellant arrived so late that his appeal had already been dismissed when he turned up. However, since it is important not only that justice should be done but also that it should seem to be done, his case was reheard. He had twisted his ankle, also six months ago, and he, too, was held to be suffering from "no loss of faculty." A wasted morning? Not if you recall what would have happened under the old scheme. Then each case would have occupied a county court for half a day. There would have been a barrister and two medical witnesses on each side, and, whatever view the court might have taken, the claimant at least would have been convinced by his advocate that he was in a bad way. Each case brought under the Workmen's Compensation Act was surely an abscess in the body politic: let us hope that we have found a new social chemotherapy.

* * *

It is a thousand pities
And one of the worst of menaces
That all committees
—By a sort of parthenogenesis—

Almost at once and as if to prove their worth
And quite impervious to snubs
Give birth
To not less than four little subs.

Wherefore I have sometimes thought
That it might be very nice
If each newly formed committee could be caught
In time, and fitted with a suitable contraceptive device.

* * *

C'est le premier faux pas qui coûte.

Digitized by Google

Letters to the Editor

ACADEMIC FREEDOM AND THE HEALTH ACT

SIR,—In your issue of Nov. 27 Professor Dible expressed the alarm which the National Health Service Act had created amongst medical academic workers. He particularly emphasised that the involvement of these workers in the working of the Act had no real connexion with academic function, and that the Act threatened both academic standards and academic freedom. The views expressed by Professor Dible were serious enough in themselves but they reflected only one aspect of the destruction of academic and professional values which the National Health Service has brought about. The nationalisation of medicine has involved the whole of our professional machinery, it has meant that clinical education has become subservient to the State and that the Royal Colleges have lost their real independence in relation to professional and educational standards.

The Central Health Services Council has upon it the presidents of three Royal Colleges, the chairman of the British Medical Association, the president of the General Medical Council, and the chairman of the council of the Society of Medical Officers of Health. The other thirty-five members are Government nominees. Not content with this, the Government has reserved powers to suppress the annual report which the council has to make to Parliament. The present chairman of the Central Health Services Council is Mr. Fred Messer, Labour M.P. for Tottenham. In a report of a recent speech of Mr. Messer's there is the remarkable statement that "For too long the needs of the people have been subservient to the needs and training of the doctors." If this is the opinion of the chairman of the council, what are the views and reactions of the three presidents of our Royal Colleges who are on a packed council? It is quite clear that, in view of the composition of the Central Health Services Council, its relationship to the Government, and it subservience to a political chairman, it has put the presidents of the colleges in a position that is both false and ignominious. Such a position of political tutelage will destroy the professional and educational independence of the colleges.

The colleges have imperilled their value and functions by their relationship to the Central Health Services Council and dependence upon the politicians. I believe, however, that the position is one which will prove to be untenable in the near future. The increasing subservience of the Royal Colleges to the politician has already had some disquieting effects. It was certainly the factor that led to the suppressions of the opinions of the fellows of the Royal College of Surgeons referred to in your columns in a letter of June 19 of last year. What is the present financial relationship between the colleges and the Government? In the case of the Royal College of Surgeons there have been persistent rumours in the profession that financial assistance has been or was about to be given. A year ago I made considerable efforts to find out from the secretary of the college whether these reports were accurate or not. The secretary refused to give any information on the matter. If any of the Royal Colleges have at the present critical juncture received Government assistance, then it creates a state of affairs of unprecedented gravity and nightmarish vistas.

What are the implications of the State monopoly of all the undergraduate and postgraduate institutions of clinical instruction? This monopoly means that every recognised teacher of medicine in this country must be a State servant. Only Government clinicians may teach clinical medicine. Such a state of affairs has no counterpart in any of the other university faculties, but it had its counterpart in the German universities. In this country it is really comparable to the old religious tests. What of the position of the medical professors and other academic workers? These workers have been involved in the vast administrative machine of the Health Act. But the function of the university worker is a function in relation to learning and not to the Government or even to regional administration. Academically, there is no greater reason why a regius professor of physic should be a regional adviser and administrator in his subject than that a professor of English literature should be a regional adviser and administrator in English. To confuse academic and administrative functions in this way is to invite disaster to higher education.

The inevitability of subservience of medical, professional, and educational institutions under nationalised medicine must have been foreseen by the leaders of the profession. Dependence on the State and subservience to the politician have replaced the valued independence of our institutions. Academic workers and teachers must be free from political control and from State coercion. Throughout the profession there is now an atmosphere of general despair at the position created by the present Act. The situation in which our Royal Colleges have been placed is a shameful one, and the only really logical course is for them to move their headquarters into the Ministry of Health itself. Such a course would have the advantage of "administrative convenience" beloved by the planners. As long as the present state of affairs exists I shall certainly not trouble to vote for elections to the council of the Royal College of Surgeons, however distinguished the names of the surgeons that appear on the ballot paper. If the present position cannot be rectified, then it will be necessary to create colleges in the future which are both independent of the Crown and independent of the politician.

London, W.1. REGINALD T. PAYNE.

TRICHLORETHYLENE AS AN ANALGESIC IN LABOUR

SIR,—I read with some surprise your summary of the findings of the committee of the Royal College of Obstetricians and Gynæcologists (Feb. 19, p. 312). The committee seems to have magnified unduly the potential dangers of the Freedman method. A study of 2354 cases yielded no evidence of increased risk to mother or child. Two observers thought that the unsupervised midwife might give the drug for longer than was customary in the series; but if this is a real danger, it could be pointed out to midwives, who are, after all, accustomed to responsibility. The second objection is that the fœtal heart-rate is occasionally affected; but there was no increase in fœtal mortality or in the interference-rate, and it is noteworthy that of the 18 cases of fœtal distress 11 were in one of sixteen hospitals.

The indefinite observations of the research fellows of the Association of Anæsthetists invite comment. Domiciliary obstetrics is conducted at a room temperature the upper limit of which is decided by comfort, or else by economic factors. This temperature does not vary more than that of a hospital labour-room, from time to time and season to season. One might ask how much shaking is required to produce an undesirable concentration of vapour. Does the bottle have to be subjected to violent agitation or is the shaking that will occur in domestic surroundings sufficient? The variations in effect due to differences in tolerance and in depth of respiration must have been observed in this hospital series; yet no ill effects are ascribed in the report to these variations, and there is no reason to think that they would cause trouble in domiciliary obstetrics. Stupor and lack of coöperation are seen in normal obstetrics and in women receiving drugs other than trichlorethylene. Before such difficulties are accepted as objections to the trichlorethylene inhaler it must be shown that their frequency is higher than in normal patients who do not receive trichlorethylene, and that the remedy is beyond the resources of the midwife, necessitating medical aid. I agree with your comment that the midwife is more likely to give too little of the drug than too much.

In his letter Dr. Freedman states that the rational course is to carry out an investigation in domiciliary practice. Though more difficult than a hospital investigation, this would be much more to the point. Hospital and domiciliary obstetrics differ in many respects, and particularly in regard to pain in labour and its relief. Supervision of the test would be necessary, and it is hard to see how this could be provided through the normal obstetric service as run by the local authorities, since

Digitized by Google

the midwives are seldom under any supervision when conducting labours. But now that the National Health Service has provided an alternative obstetric organisation, using the same midwives, the problem could be approached from a different angle. Practitioners who undertake obstetric services could provide both the supervision and the observations necessary for an investigation, and twenty practitioners from selected districts could, in two years, provide valuable information.

It would be a great pity if the Freedman inhaler were to be condemned without a further and more appropriate trial.

Bedfont. P. W. HOPPER.

PYLORIC HYPERTROPHY WITH EOSINOPHIL INFILTRATION

SIR,—In the issue of Dec. 25 Dr. Barrie and Mr. Anderson described a case of hypertrophy of the pylorus with massive eosinophil infiltration in an adult; and they said that they were unable to trace any published report of a similar case. The lesion must be very rare; and as I had a case with almost identical macroscopic findings and a somewhat similar microscopic appearance in the biopsy, I am sending this description to add to the evidence concerning this odd newcomer.

A housewife, aged 57, was admitted to the Radcliffe Infirmary on April 3, 1945, as an emergency. For two weeks the patient had been vomiting greenish material after eating. About the same time a stabbing upper-abdominal pain had suddenly appeared and had gradually become worse. The bowels were regular, but the motions had been scanty in the previous few days. There was no history of hæmatemesis or melæna. The appetite had been good until the onset of the pains.

Past History.—Epileptic since the age of 2. (Phenobarbitone gr. $^1/_2$ twice daily for years.)

1932: "Awoke after fit to find her eyes swollen and closed with an external strabismus; the swelling subsided but the strabismus has remained."

1942: Inpatient in the Radcliffe Infirmary. For six weeks she had had a dull aching abdominal pain starting in the right iliac fossa and passing all over the abdomen, and in the previous year she had lost a stone in weight. There was some abdominal swelling, especially in the lower abdomen, with slight shifting dullness. The notes record "ascending colon abnormally palpable." A barium enema showed no lesion. Blood-count was as follows: red cells 4,300,000 per c.mm.; hæmoglobin 90%; white cells 8000 per c.mm. (neutrophils 50%, eosinophils 12%, lymphocytes 38%). Occult blood was present in small amounts in two specimens of stool. Urine gave a trace of protein, culture showing *Bact. coli*. There was no pyrexia. The diagnosis at that time was "ascites of unknown cause." A month later the pains had disappeared.

Examination.—Temperature 99·2°F, pulse-rate 88 per min. Tongue dry; abdomen distended slightly with shifting dullness in the flanks. There was no particular point of tenderness. Plain X ray of abdomen: "Intestinal coils not dilated—opaque mass in the pelvis, probably ascites."

Operation.—On April 4, 1945, I opened the abdomen through a right paramedian incision. There was a considerable quantity of straw-coloured ascitic fluid; the peritoneal surface was normal. The omentum was fibrotic and contracted. The pylorus, the adjacent antrum, and the first part of the duodenum were hard and thickened, the lumen being considerably decreased and the affected tissue generally friable. The fourth part of the duodenum and about 2–3 ft. of small bowel were also thickened, and in patches hypertrophied, with a dull red mottling in places, loss of sheen, and loss of flexibility. The rest of the small bowel, the ileocæcal region, and the large bowel were normal. The liver and spleen were normal. Gastrotomy revealed a fixed mucosa in the region of the pylorus. My impression was that the lesion was Crohn's disease at a very high level. I took a biopsy from the thickened pyloric tissue and then, after closing the gastrotomy, performed posterior gastro-enterostomy using the most proximal healthy point of the jejunum, this being about 4 ft. from its origin.

For the first 6 days after operation the patient had a mild fever. Aspiration by Ryle's tube was necessary during this time. She then settled satisfactorily and was discharged to a convalescent home on April 16. I saw her on several occasions after operation, when she made no further complaint of abdominal symptoms. Her family doctor informs me that she is at present in perfectly good health as far as her abdomen is concerned.

Microscopy Report.—Dr. A. H. T. Robb-Smith reported that the specimen consisted of smooth muscle tissue with some adventitial connective-tissue, but no mucosa or submucosa. The muscle-fibres were hypertrophied and the interstitial perivascular connective-tissue showed a very marked cellular infiltration, predominantly of eosinophil leucocytes though a few plasma-cells and lymphocytes were present; no interstitial œdema and no granulomata were present, and the characters of the mucosa and submucosa could not be determined owing to their absence.

Only a small piece of tissue was available for microscopy in this case, and though bands of the eosinophils in the thickened pyloric region were observed no giant-cell follicles were seen as in the case reported by Barrie and Anderson. In their case the follicles were seen only in one isolated part of a very large specimen. The macroscopic findings are almost identical in the two cases.

Dr. Robb-Smith has kindly added this comment concerning the microscopy in this case:

"Examination of the muscular and submucosal tissue in operative specimens from 12 cases with pyloric hypertrophy revealed an interstitial infiltration with eosinophil leucocytes in 7; in none of these was it as marked as in the case described in this letter, nor did any of them show the specific features described by Barrie and Anderson, but in one case of pyloric stenosis associated with a duodenal ulcer, not only was the eosinophilia marked but there was considerable submucosal œdema and small areas of fibrinoid necrosis."

No blood-count was sought at the second admission in my case, but a blood-count at the time of admission 3 years previously showed an eosinophilia of 12%. The symptoms at that time suggested a similar (though milder) attack to that which precipitated her second admission and laparotomy. Barrie and Anderson's case similarly had a previous attack, which in that instance was 4 years before, and their patient also showed persistent eosinophilia in the blood-count. In my case I could trace no factor which could be said to have caused the lesion by allergy. Sound evidence of an allergic cause in Dr. Barrie's and Mr. Anderson's case is also lacking. Perhaps an allergic factor is the cause of these lesions, but at the moment there is no stronger pointer than the fact that both cases showed a blood-eosinophilia with large numbers of eosinophils in the local lesion.

Radcliffe Infirmary, Oxford. G. E. MOLONEY.

DIETARY FAT

SIR,—I was interested in Dr. Leitner's reply (Jan. 15) to my letter of Dec. 4.

In relation to the non-caloric functions of fat, nothing that Dr. Leitner has brought forward has invalidated the factual correctness of the statements I made. Apart from one obvious misquotation, where he cites me as agreeing with him that the absorption of calcium and phosphorus depends on an adequate fat intake, I have no comment to make on his criticisms. The issue is largely one of interpretation of the available information, most of which, unfortunately, has been obtained from the study of small animals. While Dr. Leitner is convinced of the importance of these non-caloric functions of fat, I remain sceptical as to whether these must be reckoned with in practical nutrition. Until direct experimental evidence on human beings is available, further discussion is unlikely to be profitable.

These considerations, however, are becoming somewhat removed from the issues which I had in mind in initiating this correspondence. They were, firstly, whether a reduction in the habitual intake of fat of a nation or community, of the same order as was occasioned by war circumstances in Great Britain, Switzerland, and the Channel Islands, is deleterious to health; and secondly, whether communities reported to consume very low intakes of fat suffer specifically on that account. On both these questions Dr. Leitner has little to contribute. He repeats that the intake of fat should not be reduced much below the normal established habits, yet is unable to show that, where this has taken place, there have

Digitized by Google

been ill effects. His opinion, incidentally, is at variance with that of Professor Fleisch,[1] who concluded from his experience of rationing in Switzerland that the high pre-war consumption of fat (100 g. and more per day) was unnecessary. Dr. Leitner appears to ignore the fact that man can live in good health on diets containing very little fat; indeed, the instances I provided on this score in an earlier letter (Sept. 18) he brushed aside as being of "little help in establishing our minimum requirement." It is surely only the sifting of evidence bearing on these issues that is of value in seeking to determine the minimum human requirement of fat.

Mitchell[2] in a striking paper has provided very interesting evidence for the view that, within limits, man can adjust himself to lower levels of nutrition, and that when such adjustment has taken place the body may reasonably be regarded as adequately supplied with food. In the above-mentioned countries it is apparent that a successful adaptation was achieved in changing from a relatively high intake of fat to one which, although lower, is still greater than what seems to be the minimum requirement.

Finally, in order that there should be no misapprehension, I should like to repeat that I am certainly not advocating the use of diets low in fat. But there is surely some comfort in knowing that, according to the available evidence, an involuntary reduction in the intake of fat, within limits, is not injurious to health.

Nutrition Unit, Council for Scientific and Industrial Research, South African Institute for Medical Research, Johannesburg. A. R. P. WALKER.

VEGANIN

SIR,—Dr. M. C. Macqueen (Feb. 19) comments on the quicker rate of disintegration of 'Veganin' as compared with tab. codein. co. I have confirmed this by immersing samples of the two preparations simultaneously, both in tepid water and in a specimen of gastric juice (pH 5·8). The observation, however, is irrelevant, because tablets containing aspirin should be thoroughly pulverised before they are administered. Important gastroscopic studies on this subject have been published.[3]

The rate of disintegration of a tablet is not the only factor influencing the rate of absorption of its constituents. The sole qualitative difference between tab. codein. co. and veganin is that the latter is stated to contain codeine (solubility 1 in 120) whereas in the official preparation the alkaloidal salt is used (solubility 1 in 3). If Dr. Macqueen is concerned about the rates of absorption of the two preparations, solubility is much more to the point than speed of disintegration of the tablets; and he has unwittingly raised an issue which argues the superiority of the official preparation.

Dr. Macqueen admits that it is not easy to provide evidence of the superiority of veganin over tab. codein. co. The following data may help to resolve the difficulty:

	Tab. codein. co. (grains)	*Veganin* (grains)
Aspirin	4·0	3·855
Phenacetin	4·0	3·855
Codeine	0·096*	0·117

* As codeine phosphate 0·125 grain.

Compared with tab. codein. co., a veganin tablet contains a minute excess of codeine (gr. $^1/_{50}$) and a little less aspirin and phenacetin (gr. $^1/_7$ of each). Having regard to the ordinary doses and the pharmacological actions of the constituent drugs, and taking into consideration the many variables in clinical practice (body-weight, rate of emptying the stomach, pain thresholds, &c.) is it seriously suggested that these quantitative differences have any therapeutic significance? A clinical pharmacologist must be permitted to doubt if there is any need to undertake a therapeutic trial of the two substances. Notwithstanding Mr. Eliot Warburton's indignation (*Lancet*, Dec. 4), I shall continue to teach that the only material difference is that whereas 100 tab. codein. co. cost 4*s.* 6*d.*, the same number of veganin tablets cost 8*s.* 5*d.*

Department of Materia Medica, University of Glasgow. STANLEY ALSTEAD.

1. Fleisch, A. *Schweiz. med. Wschr.* 1946, 889.
2. Mitchell, H. H. *J. Amer. diet. Ass.* 1944, 20, 511.
3. Douthwaite, A. H. *Brit. med. J.*, 1938, i, 1143. Douthwaite, A. H., Lintott, G. A. M. *Lancet*, 1938, ii, 1222. Hurst, A., Lintott, G. A. M. *Guy's Hosp. Rep.* 1939, 89, 173.

TUBERCULOUS LYMPH-NODE PERFORATION INTO BRONCHI

SIR,—In your review (Jan. 29) of my monograph *Die automatische, endogene, lymphadeno-bronchogene Reinfektion in der Initialperiode der Tuberkulose* no mention is made of lymph-node perforations into the bronchial system, though the whole work is consecrated to this phenomenon.

In the initial period of tuberculosis, swollen and necrotic hilar and parabronchial lymph-nodes perforate into the bronchial system, destroying the bronchial wall and emptying their contents into the bronchi. Thus are formed typical pulmonary infiltrations, and sometimes also cavities. Necrotic lymph-nodes often perforate also into the pleural, mediastinal, or pericardial spaces and into the œsophagus. These findings are based on 213 cases examined by myself, 85 of which are recorded in the monograph in the form of a table. The monograph contains 106 illustrations, 88 showing lymph-node perforations into the bronchi and their consequences in human phthisis.

University of Istanbul. PH. SCHWARTZ.

A REGENERATION SUBSTANCE?

SIR,—Shortly before the war I made an interesting observation in my hospital in Solo (Soerakarta, Java) which in my opinion may be of some interest to workers in the field of antibiotics and related subjects. Unfortunately I must quote from memory; for I lost all personal papers by war and internment, and Solo is still inaccessible owing to the present political disturbances.

My patient was an old man with a bedsore in one gluteus maximus so extensive and deep that my nurse was eventually able to put her whole fist in it. For about four months we tried in vain to cure this wound. Then one evening I read in the Danish journal *Politiken* an article on A. Gurwitsch's discovery of rays emitted by sprouting roots that should induce increased mitosis in other living tissues in their neighbourhood. I procured some sprouting roots by putting some Katjang-idjoe seeds between two thin layers of cotton-wool, then damped and left them overnight (just as schoolboys do to observe germination in yellow peas). The following morning I had germinated embryos. Now I cut a square off the cotton-wool layers with the embryos and put it into the wound. When, four or five days later, my head nurse and I took off the bandage, we got a surprise so big that our knees were shaking. The wound was filled to the brim with granulations: the only thing missing was epithelisation, but this followed shortly afterwards.

Katjang-idjoe—literally translated, "green beans"—are the ripe seeds of *Phaseolus radiatus* Linn., a dwarf relative of the European runner-bean, with small, globose, green seeds, much like, but smaller than green peas. These seeds are an excellent food, and are known all over South-East Asia (e.g., in Burma as "green gram") as a remedy for beriberi, owing to their high content of vitamin B_1. Moreover, young seedlings, gathered three or four days after sowing on a wet cloth and cleaned of the empty seed hulls are, under the Chinese name of Tao he, a well-known vegetable here.

About two years after this incident I met the late Ir. Booberg (director of an agricultural research station), who died during the war. He told me that in his opinion the observed phenomenon was presumably due to auxins. In the light of recent research by Boysen-Jensen and others, however, auxins—i.e., plant hormones, generated in one part of the plant, transported by the sap, and acting on another part—can scarcely be in play here, as the seedlings were not crushed. The substances in question must be secretion or excretion products of the roots.

That roots can produce biologically active material was confirmed to me by Prof. Grevenstuk, pharmacologist at the University of Batavia, who in 1939, on a visit to the late Prof. Funke, then plant physiologist at the University of Ghent, saw there demonstrated how European beans, germinating on a wet cloth through which clean water was slowly moving in one direction by capillary force, influenced the germination of seeds of the same kind, sown a few days afterwards at their side. The seeds upstream, which got the fresh water, germinated normally, whereas those downstream,

Digitized by Google

drenched with water containing the root secretion-products of their older brethren, remained stunted or failed to germinate at all. This is probably an instance in higher plants of survival of the strongest firstborn by means of an antibiotic directed against the weaker rivals of the same species. Whether this substance and the substance acting in my own experiment are of the same character, or even perhaps identical, is still unknown, but I think this question may be readily answered experimentally.

With regard to the clinical facts observed, it is perhaps best to give the wound-healing substance the provisional name of regeneration substance. In my patient the wound was so quickly filled with cells that at first I was afraid I had brought about a malignant growth. Since then I have used the same treatment on several occasions with good results; I noticed that if the wounds were infected the treatment sometimes quickly caused a greatly increased flow of pus.

This observation is published in order to stimulate other workers who are in more favourable circumstances for serious research to give their attention to this question, which seems to open up many new possibilities.

Tjikini 74, Batavia-C., Java. A. P. N. WEDEL.

*** We showed Dr. Wedel's letter to Professor Pulvertaft, of the Westminster Hospital medical school, who kindly provided the commentary which follows.—ED. L.

Since it is well recognised that the nature of the bacteria of soil is of primary importance in plant nutrition, it seems plausible to suggest that certain plants might have developed a mechanism controlling bacterial growth through their roots, either by discriminatory enhancement or inhibition. Soil bacteriologists have in fact stated that the flora adjacent to roots differs qualitatively from that in the soil more distant from them; indeed, since the physical conditions around roots must differ in many ways from those of the general soil, some kind of change in soil flora might be expected.

For some years I have tried to establish the presence of an antibiotic mechanism of this kind, but without success. In the first group of experiments plants were grown for weeks or months by the so-called "hydroponic" technique—that is to say, in dilute solutions of essential salts, aerated by a pump. The plants included peas, beans, potatoes, lettuce, and many others. At weekly intervals the fluids in which the roots were growing were tested for bacterial inhibition or enhancement. In no case was it detected. In a second group of experiments certain seeds were germinated on moist cloth, and the fluid expressed from the cloth was tested with negative results.

If roots, or indeed any parts of a plant, are crushed, the fluid obtained produces a very great enhancement of bacterial growth when tested on shake cultures, using cylinders, as in penicillin titration, especially when plates are crowded. Boiling the extracts does not destroy this property. However, exactly the same type of result is found when extracts of boiled yeast are used, and the phenomenon is surely to be explained by the action of the complex growth factors originally known as "Bios," and now very fully analysed. As a matter of general interest it may be said that folic acid, when tested in this way, produces no changes, and 1% ascorbic acid a marked ring of bacteriolysis around a zone of enhancement.

Since results of medical interest were sought, the test organisms were *Staphylococcus aureus* and *Bacterium coli*. The negative results do not, of course, prove that roots secrete no antibacterial substances; roots cannot be assumed to have humanitarian objectives. From an agricultural point of view the root fluids should have been tested on soil bacteria.

Dr. Wedel quotes an authority as stating that seeds will not germinate well in fluid in which others have germinated. For this there are many possible explanations, such as changes in pH; but an analogy exists in my own observations on bacteria grown in a flowing medium in a series of glass bulbs connected together. However rapidly the medium flows, the total growth is always maximal in the first bulb, and minimal, indeed very scanty, in the last.

There are a great many plants in the world; I remain intuitively convinced that some of them must have thought of a way of controlling their bacterial environment, otherwise than by symbiosis. I can recommend this type of research to all bacteriologists; personally I grow melons, as controls on soil in my experimental greenhouse, and can claim that not all my results are disappointing.

R. J. V. PULVERTAFT.

PALLIATIVE SURGERY IN FACIAL PALSY

SIR,—In his letter of Feb. 19 Dr. Ritchie Russell has put forward a timely warning against unnecessary operations for facial paralysis, but he weakens his case by asserting that complete unilateral facial paralysis is not always disfiguring.

Many unnecessary operations on the facial nerve have been undertaken in the past because of the failure to distinguish between degenerative and non-degenerative lesions; the rapid recoveries sometimes claimed for decompression in Bell's palsy cannot be due to regeneration of the nerve-fibres. The real problem, however, concerns the prognosis for spontaneous recovery in the presence of a known degenerative lesion. Here confusion is inevitable unless facial palsy due to injury or disease in the temporal bone is considered apart from Bell's palsy. Decision for operation in degenerative lesions from trauma or mastoid disease involves consideration of the nature of the injury or disease, the time and mode of onset of the palsy, and the condition of the middle ear and labyrinth. These otological findings can be reinforced by such evidence as may be obtained from electromyography—repeated observations being necessary at times.

Otologists concerned with the treatment of facial paralysis are well aware that the result after regeneration of the nerve, whether this occurs spontaneously or after nerve-grafting or neurolysis, can never be perfect. Symmetry is marred less by mass movements, which are often minimal, than by wasting of individual muscles during denervation. Assistance from neurologists as to the best means of limiting this wasting would be welcomed.

I agree with Dr. Ritchie Russell that further research on the natural history of facial palsy, particularly with reference to the pathology of Bell's palsy, is needed. Such an inquiry into the onset and course of the condition would be valuable in view of the paucity of post-mortem observations and the varied findings reported at operation. There is growing suspicion that a virus infection acting on the nerve from the facial nucleus or the geniculate ganglion may be responsible for many cases of spontaneous facial paralysis.

London, W.1. JOSEPHINE COLLIER.

PROPHYLAXIS OF OPHTHALMIA NEONATORUM

SIR,—Your annotation of Feb. 19 on this subject was most interesting. At this hospital—a maternity hospital used in training pupil midwives and medical students—this neonatal pædiatric problem has been a source of some anxiety.

From March, 1947, until November, 1947, using a drop of 1% silver nitrate as a prophylactic, of 1356 newborns 223 (16·5%) were noted to have a discharging eye on at least one occasion. Not all cases needed treatment, for pathological investigation showed epithelial debris only, or pus cells, and in some cases organisms (mainly staphylococci).

From November, 1947, until October, 1948, penicillin eye-drops (2500 units per ml.) were used prophylactically in 1750 births, and 266 (15·2%) of the infants were noted to have a discharge.

It was then decided to use no prophylactic eye-drops, and from October, 1948, to February, 1949, of 713 newborns 58 (8·2%) were noted to have a discharge. In this series our routine has been to do nothing at all to the eyes or eyelids at any stage in the first 6–12 hours. In the cleaning-up process which is then pursued (if the infant's general condition allows) the eyelids only are cleaned if necessary, but no drops are instilled. The infant is kept under daily pædiatric supervision, and if

Digitized by Google

a discharge develops it is barrier-nursed, the organism present determined, and treatment instituted.

Although the above series are relatively small, it is felt that the results are somewhat suggestive. The following reasons may be advanced for not performing any prophylactic procedures to the eye:

1. Although eye-drops as dispensed can be taken as sterile, after continual use from a given container their sterility is doubtful. Such drops must be changed most conscientiously at regular intervals.

2. With most eye-drops, especially if inadvertently used liberally, a reactive conjunctivitis can easily be produced.

3. Nowadays the gonococcus is relatively seldom seen in ophthalmia neonatorum, and when present its treatment does not entail the prolonged and vigorous procedures of former days.

4. It is impossible to ensure that all personnel are sufficiently gentle with, and have adequate respect for, the mucosæ and conjunctivæ of the newborn child.

I should like to thank Dr. A. G. Watkins for his encouragement and advice.

St. David's Hospital, Cardiff. J. JACOBS.

A PICTURE SOUGHT

SIR,—The picture about which Dr. Terence East inquired in his letter last week was a poster extensively exhibited on walls and hoardings, as an advertisement of Eno's 'Fruit Salts.' It was labelled, if I remember correctly, "A Wayside Consultation" and depicted, as Dr. East states, two horsemen in 18th-century dress. One, the doctor, smart and well turned out on a spirited hack, is feeling the pulse and inspecting the protruded tongue of a woebegone drooping countryman astride an appropriately sorry nag.

I cannot say when the advertisement disappeared from the hoardings, but it was certainly conspicuous up to about 26 years ago; for at that time I was giving a course of lectures on gastro-enterology, and I recommended the class to inspect the picture as a fine example of the facies of carcinoma of the stomach!

London, W.1. ADOLPHE ABRAHAMS.

URÆMIA FOLLOWING ANÆSTHESIA

SIR,—In connexion with the articles by Goodier and Goodhart (Jan. 29), and by Hewer and Woolmer,[1] and views expressed in the discussion of my paper at the Royal Society of Medicine [2] which ascribed to 'Myanesin' the potentiality for causing uræmia, I would ask leave to record the following case, which I observed a few weeks ago while working in the Kantonsspital of St. Gallen, Switzerland.

The patient was a man in a satisfactory general state, suffering from hypernephroma. Renal condition was good: blood-urea 32 mg. per 100 ml. Water excretion test: 1800 ml. in 12 hours with a range in specific-gravity of urine from 1002 to 1022.

Twenty minutes after the operation of nephrectomy was commenced, a sudden grave hæmorrhage (estimated at about 2 pints) occurred, rendering the patient profoundly shocked. Resuscitation was instituted forthwith and the blood-loss rapidly replaced by transfusion. The operation was completed as quickly as possible and the patient returned to bed still suffering from shock, from which he made a slow but effective recovery, the blood-pressure rising to 130/80 mm. Hg by next morning. After 3 days, however, the patient developed uræmia with a blood-urea of 170 mg. per 100 ml. Peritoneal dialysis was instituted, and during the next few days 300–400 mg. of urea was recovered. In spite of this the uræmia proceeded to a fatal termination, accelerated by cardiac failure and pulmonary œdema, on the 9th day. At post-mortem examination the kidney showed the typical appearance of "crush syndrome" or traumatic uræmia—a classical case in every detail.

I have always contended that shock and/or hæmorrhage was the cause of the uræmia in those reported cases which appeared that the controversial substance, myanesin, had been used in the anæsthesia technique; I have recorded such a case in the paper referred to above and gave my opinion that these were cases of traumatic uræmia from shock and unconnected with the anæsthesia.

The anæsthesia technique in the case here detailed was: thiopentone 1·5 g., nitrous oxide and oxygen, curare 12 mg. No myanesin!

I have just received details from a colleague at the Swiss hospital of a similar case, anæsthetised by the same technique, in which profound postoperative shock was followed by the same train of symptoms leading to uræmia. This patient was still alive at the time of writing, and my colleague writes: "I believe that this case also falls into the class of crush-syndrome" (translated from German).

London, W.1. F. BARNETT MALLINSON.

A FACULTY OF GENERAL PRACTICE

SIR,—The suggestion of "F.F.G.P." in your last issue calls for careful consideration; but why not a Royal College, and put it on an equality with the other three? The G.P. has become a specialist with every other member of our profession, and for this reason he needs one. Its first business would be to lay down in the widest terms what are the functions of the family doctor, and then to decide how they are to be carried out, with the ever-changing phases of our knowledge of disease, of disease itself, and of the therapeutic measures we have for their relief.

Next this college should deal with terms of service for the family doctor—a service which varies between north and south, between town and country, and between the mountains and the plains. An experience in the London Insurance Committee led me to the conclusion that you never can and never will compensate for bad terms of service by increased payment, and that men who are discussing both at once cannot and will never be able to keep the two distinct. "Settle the conditions first, and deal with the pay after, you will then be much happier." [1] Therefore the body that has to discuss with the Ministry of Health what should be the terms of service in any area ought to be quite distinct from that which has to bargain with the Treasury, through the Ministry, for payments. The British Medical Association has proved itself to be a first-rate organisation for the latter and therefore, in my opinion, should be excluded from the former. If there were a Royal College of family doctors the four colleges between them would be able to take over the arrangements for terms of service, separately for their own members and jointly for all branches of the profession engaged in clinical medicine.

So also with the conduct of practice. Shortly after the publication of the Beveridge report it was stated that "disciplinary" measures under the old N.H.I. do not need amendment. To this my experience was totally contrary. In the first place I object to the word "discipline" as applied to any and every complaint made against a doctor. Many, when justified, were due to the conditions under which he was working. "We hear at times that doctors are not as conscientious today. Conscience cannot make up for terms of service that raise disharmonies in a man's life." [2] Many are due to loose links in the chain of responsibility, which needed inquiry not from a "disciplinary" but from an administrative point of view. These the medical service sub-committees were quite incapable of appreciating. At their best they were not good, at their worst they were beneath contempt.

They order these things best in the Army. When anything goes wrong a court of inquiry is called to see whether it was due to a loose link in the chain of responsibility, an accident, or an act of God, or whether the arrangements for two services or units to work together are not equitable to the size of the other. If in this court of inquiry presumptive evidence comes out that some individual may have been at fault, the proper authority decides whether disciplinary action should be taken.

With the formation of a fourth Royal College, some such organisation could be set up to inquire into anything

1. Layton, T. B. *Lancet*, 1943, i, 56.
2. Layton, T. B. An Industry of Health. London, 1944; p. 67.

Digitized by Google

that goes wrong in clinical medicine, or into any complaint made against a clinician. Of one thing only would they have to beware. That it could never be said of them that they formed the strongest organisation in the country, every member of which would take up the standpoint of "the doctor right every time."

London, W.1. T. B. LAYTON.

INTESTINAL DIPHTHERIA

SIR,—Diphtheria may be classified according to site as follows: (1) tonsillar and faucial, (2) nasopharyngeal, (3) anterior-nasal, (4) laryngeal, (5) aural, (6) conjunctival, (7) cutaneous and in wounds, (8) genital, and (9) intestinal. The first four are the common forms; the next four are rare; and the last is the rarest. Harries [1] says that Rolleston [2] reported some instances and mentions that he himself has observed a few. Two further cases are recorded here.

Within the last ten months two children with obstinate chronic diarrhœa have been seen at the public-health clinics in Amman. Aged between 3 and 4 years, they had both had tonsillitis (but not definite diphtheria), followed by diarrhœa, of several months' duration, which resisted all treatment. They were greatly emaciated, marasmic, and toxæmic, with fever, colic, and tenesmus; they passed frequent loose stools containing blood-stained mucus and shreds of membrane.

Examination of the fæces, by Mr. Boulos Shamyeh, revealed no pathogenic organism, but the presence of *Corynebacterium diphtheriæ* was suspected. Repeated cultures revealed that this organism was actually present; no virulence test was done. Direct smears and cultures of pharyngeal swabs were negative.

Both cases were treated in the Government Isolation Hospital, Amman, with 10,000 units of antidiphtheritic serum and 100,000 units of crystalline penicillin daily for ten days. Cure was complete; and the children remain in good health after periods of eight months and four weeks.

In each case the "tonsillitis" was presumably diphtheritic. It appears that *C. diphtheriæ* was swallowed, survived the acidity of the stomach, and grew abundantly in the alkaline intestinal contents, thus giving rise to enterocolitis.

Amman, Transjordan. DJAMIL FAÏK TUTUNJI.

HEALTH CENTRES NOW?

SIR.—Nothing could have expressed one's hopes and fears more sanely, or summarised the situation more aptly, than last week's article in the "Act in Action" series.

I can produce one more argument in favour of the "prefab" which most patients would support with a good deal of feeling. It is briefly this: to wait for anything up to three hours in a surgery without a lavatory is a nightmare to every mother with a child who needs medical attention of any sort. Many doctors' houses were built specially for their purpose, with separate entrance and accommodation for the patients. But there is often no lavatory; for nobody envisaged the need for accommodating children on prolonged visits. Such premises should be condemned outright as unsuitable for use in the service. Yet the regional medical officer who visited me on behalf of the Ministry never even looked at the waiting-room.

Prefabricated centres, with telephones and sanitary facilities but nothing else, seem to me the best solution of the immediate problem. They would meet the most pressing needs cheaply and quickly, without any pretence of possibility of becoming the "key feature in the general reconstruction of the country's health services." By way of guarantee of their temporary, makeshift nature, they could be constructed to last, say, 5–8 years, and then could be called doctors' outpatient clinics or anything else which would frankly stamp them as emergency buildings.

The main danger to the dignity of the real health centres would lie in the half-way house—that is, in any institution with ambitions beyond those of an adequate shelter and a means of putting the patient in touch with the doctor. Foot clinics and physiotherapy departments, among other refinements, represent a counsel of perfection for which we obviously cannot wait, equipped as we are. I suggest that a humble structure with a humble aim would do more to pave the way towards the ideal health centre than any other form of experiment; its very cheapness and inadequacy would ensure that it could never be mistaken for a health centre; yet its usefulness—to both doctor and patient—would be abundantly clear from the start. Quite incidentally, it would give patients a hint of the potentialities of a public health service and teach them how to use it. The concept of a true health centre is not likely to dawn on them at present; their main preoccupation is how to avoid surgeries, not how to make use of them to their best advantage.

PRACTITIONER.

1. Harries, E. H. R., in British Encyclopædia of Medical Practice. London. 1937; vol. 4, p. 83.
2. Rolleston, J. D. Acute Infectious Diseases: A Handbook for Practitioners and Students. 2nd ed., London, 1929; p. 1.

STREPTOMYCIN IN WHOOPING-COUGH

SIR,—Dr. O'Driscoll reported last week a case of a boy of 9 suffering from whooping-cough and pneumonia that had failed to respond to sulphonamides and penicillin. Streptomycin was then administered and there was immediately a remarkable improvement, the right lower-lobe pneumonia clearing radiologically within four days.

A lobar pneumonia that clears so quickly radiologically suggests that the condition was fundamentally one of lobar collapse, which would not necessarily respond to chemotherapy. Collapse is known to be a frequent complication of whooping-cough, and in its early stages may clear very rapidly.

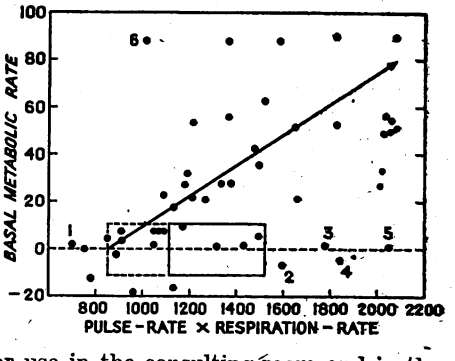
Before streptomycin is accepted as a panacea for all the ills of whooping-cough I suggest that its effects on the lung pathology be considered as possibly second-hand, or even that such changes may be unrelated.

London, S.W.1. DAVID P. NICHOLSON.

CLINICAL ESTIMATION OF BASAL METABOLIC RATE

SIR.—I welcome the comments on my article of Jan. 22 because they give me the opportunity to point out facts which had to be omitted to save space.

The chief basis of criticism seems to be the extent of correspondence between the R.P. index and the B.M.R. as determined by gas-analytical methods. I am afraid I cannot analyse Dr. Green's results (Feb. 19) because of our different interpretation of "correspondence," in consequence of which he adopts a method of comparison which lies beyond my suggestion. The R.P. index should be regarded merely as an "indicator" which indicates the direction in which the B.M.R. is shifted, and it therefore claims only an approximative correspondence with the numerical results of gas-analytical methods expressed in percentages. It does not claim to replace the gas-analytical methods; nor do the other formulæ. Dr. Robertson (Feb. 19) rightly remarks that the R.P. index has "a certain clinical value." Its value lies in its suitability for use in the consulting-room and in the following up of treatment.



It is obvious that in cases where the respiratory or pulse rate or both are influenced by other causes than metabolic impairment (cardiac and pulmonary diseases, digitalis treatment, fever, polycythæmia vera, leukæmia, &c.) the R.P. index cannot be applied, and nor can the other formulæ. Good examples of this limitation can be found in the diagram published by Miss Lovell and Dr. Martin (Feb. 12) and reproduced (with additions)

Digitized by Google

here, where cases with B.M.R. of +90% fail to show a correspondingly high R.P. index. In one of these cases (no. 6) the R.P. index is 1000, which would suggest that at a respiratory rate of 16 the pulse-rate was 62; this would be very uncommon in hyperthyroidism of B.M.R. +90% and may be due either to some other extra-metabolic causes or to an error in the B.M.R. The same conclusion can be drawn from cases which show a normal B.M.R. but a decisively high or low R.P. index (nos. 1,2, 3, 4, 5).

This diagram also shows that most cases with normal B.M.R. are shifted to the left in relation to the frame which encloses the normal range for the R.P. index outlined by me. If, following these results, the lower limit of the normal R.P. index were reduced to 900, the number of their cases falling within the normal range would represent a remarkable improvement in the correspondence between B.M.R. and the index. This correction depends on what should be taken as the lower limits for pulse and respiratory rates. The difference in the normal range between Miss Lovell and Dr. Martin's cases and mine could be due to the different duration of the rest applied before the investigation, as Dr. Robertson wisely suggests; they insisted on 30 min. rest, whereas I insist on only 5 min. Furthermore, the points representing raised B.M.R. in their diagram are not scattered irregularly but are arranged near a line which I have tried to indicate approximately without claiming its statistical accuracy. The correction mentioned above and this line indicate that the results obtained by Miss Lovell and Dr. Martin confirm the usefulness of the R.P. index, as Dr. Jordan (Feb. 26) has noted; he shows that there is a correspondence between their results and the R.P. index in two thirds of cases, the proportion which I said in my paper could be expected.

I would like to emphasise once again the great importance of counting the respirations accurately and exclusively for this purpose, because an error of 2 or 3 respirations per min. may make the R.P. index 140 to 210 too high or too low.

London, W.8. EUGENE BENE.

MANAGEMENT OF PEPTIC ULCER

SIR,—Your leading article last week and the really excellent account (Feb. 12) in the Disabilities series, are most welcome; and I hope they will be widely noted. The truth of what they both maintain, and conversely the falsity of much of the more traditional view, is manifest to anyone who is obliged to learn to live with a peptic ulcer.

Perhaps the most unfortunate result of acceptance of the conventional view of treatment is to be seen in the practitioner's surgery. Here you find a considerable number of patients whose lives are being made dreary, difficult, and even largely sterile of effectiveness and enjoyment by "unnecessary deprivations" and a preoccupation with rules and regulations of régime. "Of course, doctor, I can't eat meat, and fish is so monotonous"; "I would like to smoke sometimes, but I'm afraid to do it"; these and similar confessions by anxious-faced men, who consume huge quantities of alkaline powders and paraffin, are almost the rule.

Now the sad part of all this is that these patients have nearly always derived this anxiety and these notions from the wards and outpatient departments of the hospitals where their ulcers were originally diagnosed radiologically and treated. It is then in vain for the G.P. to say to them: "Look, I too have an ulcer, and I can assure you, from what I know to be true, that you will lead a happier and a more effective life if you forget all this, and merely avoid excesses, eat regularly, and cease to regard yourself as a disabled person." This line of talk is generally greeted with a polite smile of disbelief and a request for some more powder, sometimes even reinforced by producing a printed diet sheet, presented by the hospital. This document probably bears no sort of relation to present-day reality, and is thus a source of further anxiety and sense of guilt on the part of the patient.

These poor people are the victims of a wrong approach to the disease. In the present state of our knowledge, no sort of régime or treatment protects the man with an ulcer from the probability of periods of pain. Most ulcer patients are quite intelligent enough to be told this in a general way, and it is far more conducive to their health, in the broadest sense, to be taught to accept this position philosophically, than to be frightened into anxiety by the implanting of a belief in a lot of ineffective and galling restrictions.

Windsor. D. H. BELFRAGE.

MESENTERIC ADENITIS

SIR,—In his letter of Feb. 26 Dr. Bosc inquires about the state of the mesenteric glands in ileocolic intussusception. In my experience of this disease in infants enlargement of the lymphatic glands is a constant finding at operation. The nodes are variable in size and can be traced upwards along the line of the branches of the superior mesenteric vessel to the duodeno jejunal junction; another feature is, of course, undue mobility of the ileocæcal region. It is surprising that the known recurrence of intussusception after operation appears to be so rare, considering that the operative reduction per se presumably does not disturb the possible primary ætiology.

It is doubtful whether the enlarged nodes of acute non-specific mesenteric adenitis on the one hand, and those of acute intussusception on the other, are related, as there are points of difference between the two diseases, not the least of which is the discrepancy in the age incidence.

London, W.1. VALENTINE A. J. SWAIN.

MYASTHENIA GRAVIS

SIR,—I have read Dr. Viets's letter of Feb. 26 with great interest, and, as the author of the Disabilities article of Jan. 29, I should like to answer the points he raises.

First, the injection material I prepared was, of course, filtered. I stated in my article that "I hit on the idea of dissolving tablets *and filtering them*. . . ." Secondly, I have never been able to get as good a result from tablets as from injections. Spasm of the œsophagus is almost unavoidable with as little as two tablets, and the increase of strength after this dose is very much less than after 1·0–1·25 mg. subcutaneously. Thirdly, I can assure Dr. Viets that, in spite of my fourteen years on neostigmine ('Prostigmin'), during which I have acted as my own guineapig, I still get colic sometimes unless I take my very small doses of atropine as well. My present dose is the result of a great deal of trial and error. I have only tried to describe my own experience, and other patients must of course follow the advice of their own physicians.

On the question of thymectomy, I understand that the results are so far quite unpredictable. The failure of deep X rays to help me is not encouraging. I notice that Dr. Viets advised the operation to 30 only of his 250 patients. The fact is that I manage so well with my present treatment that I am not tempted to undergo a major operation with such an uncertain prospect.

YOUR CONTRIBUTOR.

HOSPITAL BIOCHEMISTS

SIR,—I should like to criticise misleading statements made en passant by your correspondents on the above subject.

Dr. Discombe (Jan. 22) says "that all medical graduates study chemistry to about the standard required for a general B.SC.," while "the chemist has received a fundamental training in which physical chemistry plays a large part . . . and human physiology is almost completely neglected." Surely your correspondent is not unaware that an honours B.SC. (general) is a qualification in three subjects (which may be chemistry, physiology, and anatomy) requiring a distinctly higher standard of knowledge than do the corresponding examinations in the medical course.

"Clinical Biochemist" (Dec. 18) wrote that he has "yet to meet the university graduate in chemistry who is better technically" than a fellow of the I.M.L.T. This may be so, but in my limited experience the non-chemical medical man whose ability in the chemical-pathology laboratory even approaches that of a trained technician, is indeed the rarer bird.

Digitized by Google

Is it not obvious that efficient executive and technical ability, especially for posts in the borderline sciences, outweighs academic prowess? Until such time as the universities make provision for the biochemist by offering suitably abridged medical training, it would seem that for hospital chemists the paper qualification par excellence is the F.R.I.C. (branch D). However that may be, Sir Philip Panton, consultant adviser in pathology to the Ministry of Health, has affirmed that a science graduate should be in charge of the biochemistry laboratory.

London, N.W.10. D. WATSON.

Public Health

Tuberculosis in London

THE report for 1947 of the county medical officer of health for London [1] shows that the mortality-rates from tuberculosis were the same in that year as in 1946 (pulmonary 0·62 per 1000 and non-pulmonary 0·08 per 1000); these rates "for the present at least may be regarded as having reached the level to which they might have declined if the pre-war trend had not been interrupted."

The morbidity figures, on the other hand, "indicate that the over-all cost of war in terms of tuberculosis is not yet fully paid." The rate of primary notifications of pulmonary disease, after rising to 1·83 per 1000 in 1941, fell to 1·57 per 1000 in 1946, while in 1947 it rose very slightly to 1·58; the morbidity level is still more than 20% higher than it was immediately before the war. Both relatively and absolutely the incidence of pulmonary infection in children has taken a disturbing upward trend; the rates per 1000 for the 0–14 age-group from 1943 to 1947 have been: 0·85, 0·85, 0·83, 0·94, and 1·04. With regard to pulmonary disease in adults the war-time emphasis on males has disappeared and the male-to-female ratio has fallen below the pre-war level, "indicating that the pre-war excess of females in the important 15–24 age group has been accentuated and suggesting that beyond age 25, either marriage does not give so much relaxation from strain as formerly or that in the middle age groups women are now suffering from over employment and hardship during the war years."

Influenza

The number of deaths in the great towns of England and Wales in the week ended Feb. 19 was 158 (compared with 94 in the previous week); 87 of these occurred in London and the south-east. The majority of the deaths (135) were in people over 55, so there is no sign of any relative increase in the number of deaths in young people. There has been some increase in incidence in London and the south-east, but generally speaking the disease seems to be mild.

Scotland's Vital Statistics for 1948

Mr. E. A. Hogan, Registrar-General for Scotland, announced in Edinburgh last week that the total population in the middle of 1948 is estimated at 5,169,200 —an increase of 30,500 over mid-1947. This is due to a natural increase of 43,300, reduced by a net emigration of 12,800 of which 12,100 was overseas and 700 to other parts of the United Kingdom.

The birth-rate was 19·4 per 1000 population; this is 2·6 below that for 1947, but 0·2 above the average of the previous 5 years.

The death-rate was 11·8 per 1000. This is 1·1 below the rate for 1947, and 0·8 below the average for the 5 years 1943–47; it is the lowest rate ever recorded in Scotland.

The marriage-rate was 8·5 per 1000—0·1 below that for 1947, but 0·2 above the 5 years' average (1943–47) and 0·9 above the pre-war average (1934–38).

The infant-mortality rate was 45 per 1000 live births. This is 11 below that for 1947, and 14 below the 5 years' average (1943–47). It is the lowest rate ever recorded in Scotland, being 9 below the previous lowest rate in 1946. The neonatal rate was 25 and is also the lowest ever recorded for Scotland; it is 4 below that for 1947 and 5 below the average.

The death-rate from all forms of tuberculosis was 76 per 100,000—4 below the rate for 1947, and 1 below the average for the previous 5 years. The rate for respiratory tuberculosis—66 per 100,000—is the same as that for 1947, but 6 above the average for the previous 5 years.

The maternal mortality was 1·5 per 1000 live and still births. This is the lowest on record. It is 1·2 below the 5 years' average and 0·5 below the mortality for 1947. The rate is only a quarter of that of 22 years ago, and is only about half the rate experienced as recently as 1944.

1. London County Council: Report of the County Medical Officer of Health and School Medical Officer for the Year 1947. Obtainable from Staples Press Ltd., 14, Great Smith Street, London, S.W.1. Pp. 102. 2s. 6d.

Parliament

Safe Milk

IN moving the second reading in the House of Commons on Feb. 21 of the Milk (Special Designations) Bill, which has passed through the House of Lords, Dr. EDITH SUMMERSKILL, parliamentary secretary to the Ministry of Food, described it as "a triumph over ignorance, prejudice, and selfishness." It could, she continued, be regarded as an ancillary to the National Health Service Act, because it would reduce the incidence of tuberculosis and disablement, and the death-rate. She would always think of it as the "Milk (Save the Children) Bill," and she believed that most of the medical profession would do likewise.

It was a reform of great social significance. Since 1944 the number of attested herds in the country had been doubled and it now comprised 16% of the cattle population. But the cleaning up of our dairy herds, and particularly the eradication of animals infected with tuberculosis, would take many years to complete. Quicker progress could have been made by the removal or destruction of all animals reacting to the tuberculin test, but the cost and the drop in milk production which it would entail would be prohibitive. As eradication must be a gradual process it was vitally necessary that milk should be pasteurised before sale for human consumption. Today the consensus of opinion amongst responsible medical people and health authorities was strongly in favour of pasteurisation. Prof. G. S. Wilson had recently put the number of deaths due to milk infected by the tubercle bacillus at about 1500 annually, and many thousands more were crippled. Among children the percentage of deaths was ten times greater in rural areas, where more milk was drunk raw, than in London.

The Cattle Diseases Committee estimated that about 40% of our dairy cows would react to the tuberculin test, and that about 0·5 of milch cows suffered from udder tuberculosis. There were also other diseases which the Government were anxious to eradicate, such as contagious abortion and mastitis. The Government's responsibilities in this matter were greater by reason of the official encouragement given to the drinking of milk through various welfare food schemes in schools and elsewhere. Pasteurisation, if carried out efficiently and under proper conditions, destroyed all pathogenic organisms in milk. It did not make poor milk good or good milk better, but it made all milk safe. At present some 70% of the milk sold for liquid consumption in this country was subject to some form of heat-treatment. Pasteurisation had practically no effect on the nutritional value of milk.

Describing the machinery of the Bill Dr. Summerskill said that probably the first area under it might be specified in a year or 18 months, but it might take 5–10 years before the country as a whole was covered.

Mr. SOMERVILLE HASTINGS said that anyone who had seen the frustration, continued ill health, and incapacity, as well as the premature deaths, due to drinking tuberculous milk, must be keenly in favour of the principles of the Bill. He was glad that children and others were now drinking 50% more milk than before the war, but we must see to it that the milk was pure. In London 98% of the milk was pasteurised. Repeated tests for

Digitized by Google

tubercle bacilli had been made during the past four years and not one case had been found. Abdominal tuberculosis in children in 80% of cases was due to drinking milk. In 1944 London, with its pasteurised milk, had a very low death-rate from that disease among children under five—only a tenth of that of the combined rural districts.

Pasteurisation eliminated other diseases such as undulant fever, which accounted for not fewer than 500 cases a year. There were also many epidemics due to the infection of milk by those who handled it. Between 1912 and 1937 there were in Britain 115 epidemics of dysentery, scarlet fever, typhoid, and septic sore throat, involving 14,000 people, which were found to be due to milk. Only by pasteurisation could infection by such diseases through milk be eliminated with certainty. Careful as one might be with tuberculin-tested milk it might carry infection. In 1945 in London 267 churns of T.T. milk were tested and 3 of them actually contained tuberculosis germs. In Mr. Hastings's view it was much better that T.T. milk and milk from attested herds should also be pasteurised.

Dr. HADEN GUEST asked for an assurance that under the Bill local health authorities would have the necessary powers to carry out inspection. Uncleanliness on farms was still quite common. He would also like to know by what stages and in what areas this new scheme could be brought into operation.

Mr. JOHN STRACHEY, replying to the debate, said he did not pretend to know whether scientifically even T.T. milk ought to be pasteurised. Certainly this Bill made no provision for that, and he suggested that first they should pasteurise, or in other ways make safe, the 30% of milk which still could not claim to be safe in this country. Pasteurisation was known to reduce the vitamin-C content slightly, and if that could not be supplied by oranges, or by some other suitable means, that was a disadvantage; but so far as science could show this was the only ill effect. It was a gross misrepresentation to suggest that pasteurisation had any serious nutritional effect on milk. Of course it was desirable to eliminate the tuberculous reactors from the herds, but while 40% of our dairy cattle reacted to the test any drastic policy of elimination would be disastrous not only to the farmers but to the country's milk supply. The reason why this Bill did not apply to Northern Ireland was that Northern Ireland to its credit had had a similar Bill on the Statute Book for the past six years. He agreed that the medical examination of those who handled milk was a desirable objective, but he was not sure that it could be included in this Bill. The point might however be considered during the committee stage.

Adoption of Children

On Feb. 18 in the House of Commons Mr. BASIL NIELD moved the second reading of this Bill. In framing its provisions he had in mind, he explained, two principles. The first was that while the link between a child and its natural parents must never be lightly broken, in considering a proposed adoption the interests, well-being, and happiness of the child were the paramount consideration. His second aim had been to create a relationship between the adopted child and his adopters approximating as nearly as possible to the relationship between the child and its natural parents.

Turning to the provisions of the Bill he said that it was designed to make clear that an illegitimate child could be adopted by its mother or natural father either solely or jointly with their spouse. It also provided that a child living in this country might be adopted here even though not of British birth. It restricted applications, save from relatives, to those who were not less than 25 years of age or not less than 21 years older than the infant. The Bill also laid down that no adoption order could be made unless there had been a probationary period of three months during which the child had been in the care and possession of the applicant, and during which the local welfare authority had had surveillance of the case. Hitherto a probationary period had only been necessary when an adoption was arranged through a society.

To foster a natural child-parent relationship the Bill provided that the adopter and the adopted child should be deemed to come within the prohibited degrees of consanguinity, and Mr. Nield hoped that at the committee stage it would be possible to add provisions dealing with succession and inheritance which would put the adopted child in a similar position to the natural child.

On behalf of the Government Mr. K. G. YOUNGER, under-secretary of State for the Home Department, welcomed the Bill, which he thought remedied many of the serious defects in the present situation. Mr. SOMERVILLE HASTINGS considered that the probationary period was not long enough. The L.C.C. insisted on six months. They were also careful not to arrange for adoption under the age of nine months so that they could be certain the child was healthy in mind and body. Before a child was adopted, he suggested, the Court should also insist on a health certificate from the adopters. The Bill was read a second time.

Shortage of X-ray Films

On the motion for the adjournment in the House of Commons on Feb. 22, Mr. L. J. EDWARDS, parliamentary secretary to the Board of Trade, replying to Mr. Maude who raised the question of the shortage of X-ray films for hospitals, said that the annual increase in demand had risen from the normal 15% to between 20 and 25%. It had been agreed to reduce exports from 45% of output to 40%, and this would be reviewed again next June. Plans for the extension of production capacity were unlikely to be completed for 18 months or 2 years. There was a world shortage of X-ray films and it was a considerable economic sacrifice, taken in the interest of the nation's health, to reduce exports by 5%. Demand in 1949 would be 30% above last year, and production was expected to be approximately 27% higher.

Health Service Benefits for Foreigners

In the House of Lords on Feb. 22, Lord BROUGHSHANE asked in what circumstances free medical services and medical and dental appliances, such as dentures and spectacles, were supplied to foreigners visiting this country who had paid no contributions to the British National Health Service; and what was the estimated cost of providing these special privileges for foreign nationals?

The Earl of LISTOWEL replied: The Act is so framed as to cover everyone in this country, including foreigners. There are therefore no special arrangements relating to foreigners and no separate estimates of cost.

Lord BROUGHSHANE: Is the noble Earl aware that a leaflet has recently been handed to all visitors arriving at British ports stating that the National Health Service will provide them, free of charge, with any medical, dental, and nursing care during their sojourn in Britain? What is the explanation of emphasising this fact to all foreigners arriving at our shores, when they have not contributed in any way towards the expenses of providing these services and appliances?—The Earl of LISTOWEL: I am not aware of that leaflet, but I will draw the attention of my right hon. friend to its existence. At the same time, perhaps the noble Lord will realise that, as on the average foreign visitors stay here only one month, it is not likely that the benefits they derive from the National Health Service are numerous. Lord BROUGHSHANE: Is it not possible to obtain a pair of spectacles or some dental appliance even within one month? Some of us have been obtaining these things in a less period of time that that.

Lord HAWKE: Is the noble Earl aware of an allegation that Lascar crews are arriving in this country without teeth in their heads and are going back with "National" teeth and selling them in the bazaars at the other end? Lord SALTOUN: If that is so, may I inquire how these people get their teeth and spectacles so much sooner than do the people who belong to this country? No further replies were given.

QUESTION TIME

Fees for Certificates

Mr. ALBERT EVANS asked the Minister of Health in what circumstances doctors treating patients under the health service were permitted to make a charge for medical certificates.—Mr. ANEURIN BEVAN replied: A doctor is required to issue to patients under the National Health Service free

Digitized by Google

of charge any certificates reasonably required by them under or for the purposes of any enactment. A list, which is not necessarily comprehensive, of certificates which appear to fall into this category has been circulated to doctors. There is nothing to prevent a doctor making a charge for other certificates.

Allowances for Medical Treatment

Mr. NIALL MACPHERSON asked the Minister of National Insurance what provision his regulations make for payment for loss of time to persons insured under the National Insurance Scheme who have to attend for medical treatment at a hospital at weekly or other regular intervals and, in consequence, lose a day's work each time.—Mr. STEELE replied: The National Insurance Act contains no power to make regulations for the purposes mentioned. As regards industrial injuries the regulations provide that any claimant or beneficiary who is directed by the Minister to undergo medical treatment may be paid travelling or other allowances including compensation for loss of remunerative time.

Liver-extract Preparations

Major GUY LLOYD asked the Minister of Health whether he was aware of the concern of members of the medical profession at the unsatisfactory response of patients to treatment with liver extracts, due to the extracts being prepared from animal livers unfit for human consumption; and whether he would arrange with the appropriate Minister that such liver extracts should in future be prepared only from healthy animal livers, which had been properly and individually tested clinically beforehand.—Mr. BEVAN replied: I have had a number of complaints of this kind. It would, I fear, be impossible to adopt the suggestion of individual clinical tests, but I propose to consider with the Minister of Food whether any other action should be taken. The process of extraction makes the extract quite safe.

Major LLOYD: Why should livers be now taken from carcases that are entirely unfit for human consumption and used for this purpose?—Mr. BEVAN: Once more a statement is being made which may frighten those who are taking this extract. On the best advice that I have taken it appears that the extract, although it might not be effective for the purpose for which it is used, is quite safe.

Cost of the N.H.S.

Mr GRANVILLE SHARP asked the Chancellor of the Exchequer if he would now give revised estimates in terms of pence per £ in income-tax of the cost to the taxpayer of the National Health Service during the present financial year.—Mr. GLENVIL HALL: Seventeen and a third pence in the £.

Vacant Beds

Mr. J. A. LANGFORD-HOLT asked the Minister of Health how many hospital beds were vacant on Jan. 1, 1949.—Mr. BEVAN replied: On Dec. 31, 1948, there were: Beds staffed and occupied, 398,229; beds staffed and unoccupied, 56,215; beds unstaffed, 52,924.

Colonel M. STODDART-SCOTT: Will the Minister say how it is that there are 52,000 beds unstaffed at the present time when we have 35,000 more trained nurses in the United Kingdom than we had in 1938?—Mr. BEVAN: It is because we have much more hospital accommodation, many more patients in hospitals, and many more people ready to take advantage of hospital facilities.

Free Medicine for Private Patients

Mr. F. W. SKINNARD asked the Minister whether he would introduce regulations to make eligible to receive medicines and drugs free of charge under the National Health Service those private patients who were refused admission to the panel of the doctor of their choice because he considered that they resided at an uneconomic distance from his surgery.—Mr. BEVAN replied: No, Sir. Mr. SKINNARD: Is the Minister aware that very often a doctor has a good case for refusing to put a patient on the panel but in the patient's case there is a very serious reason why he should remain for a time at any rate with the private doctor of his original choice?—Mr. BEVAN: I see no point in that at all. If the doctor does not take the patient the patient should seek another doctor. That is no justification for amending the whole Act.

Ophthalmic Fees

Sir GEORGE HARVIE-WATT asked the Minister what fees were payable to persons included in the ophthalmic list for services rendered under the National Health Service; and whether he would make a statement on his negotiations in progress to adjust these amounts.—Mr. BEVAN replied: The fees are—

Ophthalmic medical practitioners, sight-testing fee ..	£1 11*s.* 6*d.*
Ophthalmic opticians, sight-testing fee	15*s.* 6*d.*
Ophthalmic or dispensing optician, dispensing fee ..	£1 5*s.* 0*d.*

Any proposals to adjust these amounts are matters for discussion with the professional organisations as regards ophthalmic medical practitioners and with the Optical Whitley Council as regards opticians.

Free Health Services for Aliens

Sir WALDRON SMITHERS asked the Minister by what authority he issued N.H.5, no. 2.—Mr. BEVAN replied: There is no N.H.5, no. 2. Sir W. SMITHERS: I have in my pocket—it is a misprint—"National Health Service No. 2," an approved paper, which is given to every alien who arrives in this country offering him free health services. Is not the Minister breaking the law in offering free health services to aliens and will he tell the House who pays for these services to aliens who can afford the fare to come here?—Mr. BEVAN: The leaflet is for the purpose of informing persons who take out identity cards in this country and seamen who missed the original distribution what they can obtain through the National Health Service. Sir W. SMITHERS: The leaflet does not say so.

Medical Treatment Abroad

Mr. W. N. WARBEY asked the Minister whether he would introduce amending legislation to empower regional hospital boards to provide or pay for treatment outside Great Britain in appropriate cases.—Mr. BEVAN replied: This is a matter for the Treasury and not for me. I certainly cannot add to the obligations of the health service by sending people abroad for treatment at this time.

Mr. P. W. DONNER asked the Chancellor of the Exchequer whether he was aware that several thousand persons suffering from tuberculosis cannot receive adequate treatment or hope to be cured in hospitals in this country owing to the shortage of beds and/or nurses; and whether he would supply foreign exchange on request to such persons in order to enable them to be cured in Switzerland.—Mr. GLENVIL HALL replied: I am aware and am sorry that there are at present long waiting-lists of patients for sanatorium treatment. I regret, however, that foreign exchange cannot be granted automatically on request to enable persons suffering from tuberculosis to go to Switzerland. The Exchange Control Medical Advisory Committee examines all applications for exchange on health grounds and advises whether the medical evidence justifies the provision of currency for treatment abroad.

Mr. RALPH ASSHETON: Is the panel allowed to take into account the fact that attention cannot be given to the patients in this country?—Mr. GLENVIL HALL: It can take everything into account.

Health Travel to Switzerland

Colonel O. E. CROSTHWAITE-EYRE asked the Chancellor of the Exchequer what was the amount of Swiss francs made available, respectively, to tourists and to those who for medical reasons had to go to Switzerland for treatment in each of the last three years.—Mr. GLENVIL HALL replied: The amount available for United Kingdom tourist expenditure in Switzerland during the 12 months ending April 30, 1949, is £5 million. It is estimated that the present annual rate of expenditure on health travel to Switzerland is about £400,000.

Scottish Marriage Guidance Council

Mr. ANDREW GILZEAN asked the Secretary of State for Scotland whether he proposed to give financial assistance to the newly formed Scottish Marriage Guidance Council.—Mr. ARTHUR WOODBURN replied: The council requires financial assistance in the initial stages of its work. I propose, therefore, to ask the House to approve a supplementary estimate to enable a grant of £250 to be made to the council during the current financial year.

Thyroid Tablets

Mr. H. LEWIS AUSTIN asked the Home Secretary if he was aware of the increased number of fatalities and serious illnesses arising from excessive use of thyroid tablets; and if he would now consider the inclusion of this dangerous drug in the restricted sale provisions of the Dangerous Drugs Acts.—Mr. CHUTER EDE replied: I am advised that thyroid extract is not a drug which would be productive of ill effects similar or analogous to those produced by morphine or cocaine and that consequently it is not a drug to which the Dangerous Drugs Acts can be applied.

Digitized by Google

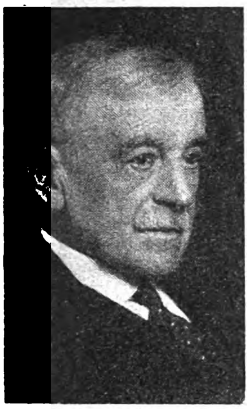
Obituary

WILLIAM HALE-WHITE

K.B.E., M.D. LOND., M.D. DUBL., LL.D. EDIN., F.R.C.P.

Sir William Hale-White, who died on Feb. 26 at the age of 91, had outlived his generation of physicians. By the end of the 1914–18 war he had already left the active staff of Guy's Hospital, and to the younger physicians of that time he was known more as a friend, and as a most helpful adviser, than as a practising and teaching physician.

His long association with Guy's began in 1875 when he entered the medical school. He graduated four years later, taking his M.D. the following year. In 1885, when he was appointed to the staff of the hospital, he was already lecturer in materia medica, and in 1899 he became also lecturer in medicine. During the 1914–18 war he acquired many other responsibilities, acting as consulting physician to various war hospitals, as a member of the Final Medical Appeal Board, and as chairman of Queen Mary's Royal Naval Hospital, Southend. After these strenuous years he retired from the hospital in 1919 and in the same year he was appointed K.B.E.



Press Portrait Bureau

Sir William's earlier writings were for his own profession and included a *Textbook of General Therapeutics* (1889), a *Textbook of Pharmacology and Therapeutics* (1901), and *Common Affections of the Liver* (1908). His best-known book, whose title *Materia Medica, Pharmacy, Pharmacology, and Therapeutics*, has been shortened to the affectionate and eponymous "Hale-White," first appeared in 1892, and its 26th edition was published three years ago. He was joint editor of *Guy's Hospital Reports* from 1886 to 1893 and in 1925 he founded the *Post-Graduate Medical Journal* of the Fellowship of Medicine, over which he presided from 1927 to 1932. He was also one of the original editors of the *Quarterly Journal of Medicine*, the organ of the Association of Physicians of Great Britain and Ireland,—a body which he served as president. At different times he presided over the Medical Society of London and the Royal Society of Medicine.

He took a lively interest in education and in the '90s contributed controversial letters to our columns on the proposed reconstitution of the University of London. As treasurer of Epsom College and chairman of Bedford College he continued long after his retirement to give his time and experience to this work. He was also a vice-chairman of Queen's Institute of District Nursing and a councillor of the British Red Cross Society.

The senior fellow of the Royal College of Physicians—he was elected in 1888—Sir William had served that body as examiner, councillor, and censor. In 1897 he delivered the Croonian lectures, on the means by which the temperature of the body is maintained in health and disease, while his Harveian oration in 1927 on Bacon, Gilbert, and Harvey, reflected the interest in medical history which enriched his retirement. In *Great Doctors of the Nineteenth Century* with understandable partiality he found many of his heroes among Guy's men, and this loyalty also perhaps first led him to make an intensive study of Keats's medical career. In *Keats as Doctor and Patient* (1938), the last of his books, he exploded many false assumptions and concluded that "all we know is that Keats was attacked by reviewers and died of consumption."

Of this later part of his life Dr. Maurice Campbell writes: "His series of articles on medical biography and history, mostly published in *Guy's Hospital Reports*, will be of the greatest value to the next historian of Guy's Hospital who tries to cover the period of history since Wilks and Bettany. They combine an accuracy of detail with a scholarly method of writing that give them great charm and make them easily and widely read, and this might be expected in the son of 'Mark Rutherford,' whose books have an almost unique charm for those who know and like them. Some of the best known of these biographical papers are on Richard Bright and his discovery of the disease that bears his name (1921), on the early papers of Richard Bright (1928), on Thomas Hodgkin (1924), on Keats as a medical student (1925), on Golding Bird and on Addison (1926); on the *Guy's Hospital Reports* (1931), and on some of the lesser-known Guy's physicians of the 19th century (1934). In a different vein was the 1930 volume on some satirical prints of Thomas Guy and on the famous forensic trial of White Webster in America.

"In stressing the historical side of Sir William's work," Dr. Campbell continues, "I would not like readers to forget the eminent position that he occupied as a clinician and consultant, as a teacher, and as a leader in the medical world. A number of the *Guy's Hospital Reports* in celebration of his 75th birthday in 1932 is entirely composed of articles by his house-physicians, and is a tribute to the influence of his teaching. He may be one of the last whose reputation will stand so high over such a wide range of medicine. He had written papers of importance on cerebral tumour, ulcerative colitis, cirrhosis of the liver, empyema, rheumatoid arthritis, and exophthalmic goitre, and on 'diseases of the heart due to over-indulgence in alcoholic drinks,' as well as the well-known textbooks. Apart from his general influence, perhaps his papers on perihepatitis and on the distinction between hæmatemesis from acute and from chronic ulcer have passed most completely into general knowledge.

"Even as he got older Sir William was a delight to talk with, and in earlier days his house was a happy centre for all who knew him. He retained an amazing interest in life; during the war he did not leave London till a large part of his house had disappeared around him, and he still paid frequent visits all through the war."

Sir William received an honorary degree from the University of Dublin in 1909, and from the University of Edinburgh in 1927, and he was elected to the honorary fellowship of the Royal College of Physicians of Edinburgh in 1931. He married in 1886 Miss Edith Fripp, sister of his colleague Sir Alfred Fripp. She died in 1945. They are survived by one of their sons, Dr. Reginald Hale-White.

Births, Marriages, and Deaths

BIRTHS

ALDRIDGE.—On Feb. 22, at Crookham, Hants, the wife of Dr. R. C. P. Aldridge—a daughter.

ASTBURY.—On Feb. 21, at Parkstone, the wife of Dr. John Astbury—a son.

BREARLEY.—On Feb. 19, at Sheffield, the wife of Dr. B. F. Brearley—a son.

CLARK.—On Feb. 25, at Northowram, Halifax, the wife of Mr. T. L. Clark, F.R.C.S.—a daughter.

CORMAC.—On Feb. 26, at Macclesfield, the wife of Dr. C. D. Cormac—a daughter

DACIE.—On Feb. 22, in London, the wife of Dr. J. V. Dacie—a son.

DOWNMAN.—On Feb. 23, in London, the wife of Dr. C. B. B. Downman—a daughter.

FYNN.—On Feb. 19, at Salisbury, S. Rhodesia, the wife of Dr. R. W. Fynn—a son.

GOWANS.—On Feb. 15, at Boston, Massachusetts, the wife of Dr. J. D. C. Gowans—a daughter.

HARE.—On Feb. 18, at Bournemouth, the wife of Dr. D. M. Hare—a daughter.

LANGDON-DOWN.—On Feb. 22, in London, the wife of Dr. Norman Langdon-Down—a son.

MALLETT.—On Feb. 18, at Wimborne, Dorset, the wife of Dr. A. E. de la T. Mallett—a son.

TAYLOR.—On Feb. 21, at Worthing, the wife of Dr. P. B. Taylor—a son.

DEATHS

EDWARDS.—On Feb. 23, Ivor Charles Edwards, M.D. Lpool, D.P.H., aged 62.

GREENE.—On Feb. 18, Helen Evangeline Elizabeth Mary Anne Greene, M.D. Brux.

JACKSON.—On Feb. 20, Robert William Henry Jackson, M.A., M.D. Dubl., major, R.A.M.C. retd. aged 84.

TOBIN.—On Feb. 23, Joseph Richard Tobin, M.R.C.P.I.

WHITE.—On Feb. 26, at Oxford, Sir William Hale White, K.B.E. M.D. Lond., F.R.C.P., aged 91.

Digitized by Google

Notes and News

TRAINING GRANTS FOR ASSISTANTS

THE Minister of Health has issued a further circular [1] to guide local medical committees in dealing with applications for a grant for training assistants. He points out that the number of newly qualified doctors wishing to be trained is likely to be only some 500–1000 per annum. This means that no more than about 5% of general practitioners will be able to secure an assistant under the scheme; and committees will thus be able to take a high standard in selecting principals for the purpose of teaching. The following are among the considerations which, it is suggested, should be taken into account:

1. The standing of the applicant.
2. The applicant's list, and also his other commitments. The size of his practice should not be too large; but he should have not less than 2000 patients on his list, except in a rural area, where the minimum is now reduced to 1500.
3. Whether the applicant is in partnership and whether he already employs an assistant.
4. The type of practice. Preference should be given to a mixed practice providing variety of experience, including obstetrics.
5. Qualifications and experience. The "trainer" should have had not much less than ten years' experience in general practice, and only exceptionally should he be over 65 years of age.
6. Premises and equipment. These should be of a high standard; and the circumstances should be such as to allow the "trainer" to exercise supervision over the assistant.

The Minister suggests that local medical committees should review at least every five years the names of doctors approved as "trainers." The assistant must not, during the period in which the training grant is being paid, apply to have his name included in the medical list.

COURSES IN NATURAL SCIENCE

CANDIDATES for entrance in science to the women's colleges at Oxford and Cambridge often have little idea, it seems, of the courses available to them at these universities. The six women's colleges in the two universities, and St. Anne's Society at Oxford, have prepared and jointly sponsor an informal account of the science courses, written by the science tutors and lecturers, which explains what each university offers and in what they differ from each other. The 12-page leaflet may be had for 1*s.* from B. H. Blackwell Ltd., at Oxford, or Bowes & Bowes, at Cambridge.

DETECTION BY TELEPATHY

Dr. David Wintringham has his hands full in the latest problem presented to him by his creator, Miss Josephine Bell.[2] He has to be up in all the latest experiments on telepathy, and to recognise the drawbacks of myasthenia gravis as well—though he was hasty in including impending death among these. (Readers with myasthenia need not feel obliged, out of respect for his infallibility, to hurry across Jordan in the course of the next year or two.) All his other assertions are faultless and lead us, if deviously, to the guilty party. A digression concerned with the well-recognised syndrome of children, caves, and tides, revived, in one reader at least, a forgotten habit of nail-biting in moments of literary excitement.

INDIAN DRUG RESEARCH INSTITUTE

NEARLY 35% of the vegetable drugs listed in the *British Pharmacopœia* are native to India, and substitutes for several others can be found among the rich and varied flora of that vast country. These resources have not been fully explored and exploited; and for some time the need had been felt for a central organisation to achieve this object. Early this year the Board of Scientific and Industrial Research decided to set up in Lucknow a Central Institute for Drug Research. In the short term, the accent will be on natural drugs, but gradually research in the fields of synthetics and antibiotics will be intensified. The institute will perform five related functions: (1) promotion of drug research in general, including botanical, chemical, pharmacological, bacteriological, microbiological, and clinical aspects; (2) testing and standardisation of drugs, and tendering expert opinion thereon as a guide for further research, development, and production; (3) offering facilities to, and helping, scientists in universities, special institutions, and industrial concerns, and others who may not be in a position to carry out investigations by themselves; (4) providing controlled clinical trials; and (5) dissemination of scientific knowledge and statistical information relating to drugs.

The institute is expected to work in close harmony with the National Chemical Laboratory at Poona. It will have a director, four assistant directors in charge of the principal divisions, and fifty technicians, apart from a number of research scholars.

REORIENTATIONS IN NEUROLOGY

ADDRESSING the Manchester Medical Society on Feb. 2 Sir CHARLES SYMONDS (London) said that the most fascinating and elusive problem of neurology was that of the selective lesion. We find this or that structure picked out again and again by different diseases in such a way, for example, that examination of the pupils alone may be warrant for the diagnosis of neurosyphilis. Of the reasons for this we know hardly anything, but it seems that it may depend on the effect of toxins, or deficiencies, on specific biochemical functions. Myasthenia gravis is the best-known example of a biochemical lesion; familial periodic paralysis and porphyria are less well understood, but of interest because of the genetic factor. Some of the obscure paralyses, such as that described by Landry, may be due to similar causes. The paralysis of botulism and the spasm of tetanus are now known to depend on derangement of the acetylcholine—cholinesterase mechanism of neuromuscular transmission. There is evidence suggesting that this mode of transmission may also exist within the central nervous system across synapses; and, if so, certain functional nervous disorders may prove to be caused by analogous biochemical disturbance.

Specific patterns of central nervous disease are related to equally specific nutritional deficiency. Subacute combined degeneration of the cord is the best-known clinical example, and the prison camps in the Far East provided others. Animal experiments have shown correlation between the histological pattern of lesions and specific vitamin deficiency, whether due to lack of vitamins or excess of antivitamins in the diet. Disseminated sclerosis remains a mystery, but the experimental production by Weston Hurst of demyelination of optic nerves and other structures in the monkey by interference with intracellular oxidation suggests the possibility of a biochemical lesion, and the familial cases may reflect an inherited error of metabolism.

Bodian and Howe have shown that the susceptibility of anterior horn cells to the virus of poliomyelitis can be modified by an artificially induced resting state following section of peripheral nerves. Bodian has further shown that the natural immunity of rhesus to oral infection by the virus of poliomyelitis is lost when the animal is deprived of pyridoxine. It seems, therefore, said Sir Charles, that we may have to think in terms of interaction between virus and metabolic disorder if we are to understand the ætiology of certain nervous diseases.

THE ASSISTANCE PUBLIQUE

A SPECIAL number of the *Presse Médicale* (Jan. 5), reminiscent of the sumptuous issues of this journal in pre-war days, is devoted in part to a description of the activities of the Assistance Publique de Paris, whose centenary occurs this year. Before the Convention (1792–93), the sick, the aged, and abandoned infants were cared for by three independent bodies. These the Convention attempted to nationalise, but the original arrangement was hastily restored. However, the idea of centralisation was not forgotten, and in 1849 the National Assembly established the Assistance Publique.

About twenty years later Maxime du Camp was able to praise the improved provision for the sick. "When one visits the hospitals," he wrote, "and sees white curtains at the large windows, beds separated and furnished with all the indispensable utensils, when one sees the neat nurses glide like beneficent shadows across the vast well-lighted wards, when one knows that the most eminent physicians and surgeons have the honour of caring for the patients, it is difficult to visualise the conditions which prevailed before the new administration took charge." Unfortunately this bright picture seems to have been dimmed during the next few years, for Prof. Charles Achard in 1937 spoke of the scene when he was a student sixty years before. "In the always congested wards," he said "beds were surrounded with dusty curtains while smoke from the stoves spread through the air and at night small oil-lamps gave the effect of glow-

1. E.C.L. 152. See also *Lancet*, 1948, ii, 656, 712.
2. Death in Clairvoyance. London: Longmans Green. 1949. Pp. 244. 9*s.* 6*d.*

Digitized by Google

worms. Poultices, heated and re-heated, emitted a sickening odour. The mortuary was often next to the operating-theatre, and, ignorant of microbes, the medical staff themselves sowed disease and death. The lying-in wards, attended indifferently by surgeons and physicians, were frequently closed because of puerperal fever. Lint, used without regard to being soiled, was the common dressing. Scarlatina and measles were nursed in the same ward, and many children, admitted for a simple measles, died of diphtheria contracted from their neighbours."

This centenary year is a milestone of progress. The vast organisation of today is centralised in Paris under a director responsible not only for 80 hospital establishments, with some 45,000 beds, but also for home nursing and the protection of infants, and the care of old people, in which it has set examples worth particular attention.[1]

NEW JOURNAL ON NURSERY SCHOOLS

IN our attempts to free the mother for industry by providing nursery care for her young children, we have not always, perhaps, kept all the needs of the child to the fore. The Nursery School Association has always stood out for the principles laid down and studied by Margaret McMillan: that the nursery school is a place where a child learns not merely to use materials but to live a social life in a group. The association has now reached its silver jubilee and has marked the occasion by publishing a new quarterly journal, *Young Children*. In a foreword, Lady Allen of Hurtwood refers to the new World Council of Early Childhood Education founded in Prague last summer. This body will work with UNESCO and the World Health Organisation, the aim being, as Lady Allen says, "to stir people all over the world to think more carefully about the better upbringing of young children and the happiness of the family." The association's address is 1, Park Crescent, London, W.1.

MEMORIES OF A SURGEON

THOSE who heard Prof. G. Grey Turner give the first Rutherford Morrison lecture of Durham University in 1947, will remember how vividly he recalled the surgery of the turn of the century and the personality of the man whom the lectureship honours. Rutherford was a questioning, dexterous surgeon, pressing forward continually to new territory, and teaching as he went. This account of him could only have been written by one who could supplement research by memory, and, for that reason, is itself memorable. It was published in the *Newcastle Medical Journal* for June, 1948, and has been reprinted.

SWEDISH PUZZLE

August Strindberg's life was a dissolving view. At one moment hailed as an advanced thinker, a faithful child of God, or a promising scientist, at another condemned as a cynic, an atheist, a reactionary, or a degenerate, he seems at once less than human and more than life size. He was in some ways all of these things, as people in the grip of a powerful neurosis often are; and he had that other quality of the neurotic: he believed intensely in the agonies he was experiencing at any given moment. For him they were a revelation of truth which must be uttered, come what might, even though they contradicted all his former findings, or betrayed to obloquy a once-loved wife or a trustworthy friend. His difference from the ordinary man or woman sick in the same way lay in his fertile power of self-expression. Far from paralysing him in action, his changing moods and beliefs drove him to write, to paint, to experiment in chemistry and alchemy, to trifle with magic, and to fret three honourable and well-intending wives into leaving him. Above all he was driven to write. Books, plays, and articles spouted from him, and this leviathan seemingly had an ocean to draw on. At the beginning of this century, when he had already turned 50, he wrote seventeen plays in five years, and still had several productive years ahead of him. Miss Elizabeth Sprigge, in writing his biography [2] has had to pack him up in less than 250 pages, an allowance which her subject would have thought meagre even for a synopsis. She has done it in sentences almost spare enough for telegrams; and with a restraint rare in biographers she offers no comment either on his actions or his feelings. It is as though Strindberg himself, somehow fitted with an impartial style, stood off and gave an account of himself in the third person. Miss Sprigge knows well enough—as far as anybody knows—how he can be labelled medically (for as she rightly points out in a postscript, we may call his state paranoia, or melancholia, or schizophrenia, or trouble with an œdipus complex, without getting much forrarder), but she never allows diagnosis or clinical interpretation to mar her faithful account of what he felt and what he did; in any case, as she says, no ready-made labels suffice. The speed and terseness of her narrative set off his luxuriance.

1. Amulree, *Lancet*, 1946, ii, 801.
2. The Strange Life of August Strindberg. London: Hamish Hamilton. 1949. Pp. 246. 15*s*.

University of Liverpool

On Thursday, March 10, at 5 P.M., Prof. E. D. Adrian, O.M., F.R.S., will deliver the Sherrington lecture in the arts theatre of the university. He is to speak on Sensory Integration.

Leeds Postgraduate Course

A refresher course for general practitioners has been arranged by the University of Leeds and will begin on May 2. Further particulars will be found in our advertisement columns.

President Truman's Social Security Proposals

Mr. Truman's programme for extending the social-security system of the U.S.A., which was introduced into the House of Representatives on Feb. 21, recommends that existing benefits be liberalised, that coverage be expanded, and that disability insurance be added to the existing old-age retirement and survivors' insurance scheme. At present there is no Federal insurance system against disability. Direct Federal contributions to States with established programmes for the needy are also proposed.

Medical Photographers

The Institute of British Photographers has compiled a report on the function of departments of medical photography in the National Health Service, and on the training, qualification, and standing of medical photographers, of whom a register is being started. To be included in the register, candidates must have practised medical photography for at least two years; and ultimately registration will depend on passing the institute's final examination in medical photography.

Care in Old Age

Speaking at a conference in Inverness on Feb. 24, Sir Andrew Davidson, chief medical officer of the Department of Health for Scotland, divided the elderly into four groups: (1) those needing hospital care; (2) those, no longer capable of leading a completely independent existence, who would be happier and more comfortable in eventide homes; (3) those living alone at home who require the assistance of home helps, cooked meals provided from outside, and voluntary workers to do the shopping, and those living with relatives who might need temporary accommodation at eventide homes during the holidays or illness of the younger people; and (4) those who are not infirm. Sir Andrew pointed out that even if only one pensioner in fifty needed residential accommodation, eventide homes would have to provide $2^1/_2$–3 places per 1000 of the population.

World Health Organisation

At its meeting in Geneva last week the executive board discussed the intended withdrawals of the U.S.S.R., the Ukraine, and Byelorussia from W.H.O. (see *Lancet*, Feb. 26, p. 355). The board endorsed the action taken by the secretary-general and agreed that every effort should be made to bring the three countries to reconsider their attitude. Among the 14 members present the only dissenting voice was that of Dr. Boguslav Kosusznik, representing Poland, who said he was in full accord with the Russian views and that he would clarify his position in the near future.

The board approved, among other things, a project by which W.H.O. would join with the Food and Agriculture Organisation in a programme for controlling the diseases and developing the agriculture of three undeveloped areas to be selected after survey. The cost of cleaning up 10 million acres of agricultural land, with unhealthy populations, is estimated at 2 million dollars a year for five years. The governments of the countries concerned would have to pledge themselves to continued and vigorous action in the areas improved. The programme will go before the Economic and Social Council with a recommendation that a beginning be made next year.

Digitized by Google

Royal Society of Edinburgh

A David Anderson-Berry medal, together with a sum of money amounting to about £100, will be awarded in 1950 for the best work on the therapeutic effect of X rays on human diseases. Applications, which may be based on published and unpublished work, should reach the general secretary of the society, 22, George Street, Edinburgh, 2, by March 31, 1950.

Dental Working Party

The Ministry of Health have appointed a Working Party to ascertain the average chairside time taken by general dental practitioners (1) in the National Health Service and (2) in private practice to complete each of the types of dental treatment set out in part I of the first schedule to the National Health Service (General Dental Services) Fees Regulations, 1948, excluding any items for which it is impracticable to establish an average time—e.g., orthodontic treatment. The Party consists of Mr. William Penman, F.I.A. (chairman), Mr. A. Macgregor, L.D.S.F.P.S., Mr. S. Donald Cox of the British Dental Association, Mr. J. Lauer, L.D.S. R.C.S., of the Public Dental Service Association, and Mr. A. H. Condry of the Incorporated Dental Society. The investigation is due to begin early in March. Dentists selected by the chairman will be invited to assist in the investigation and it is hoped that they will be willing to coöperate.

Registration of Foreign Doctors in the U.S.A.

The Federation of State Boards of Medical Examiners, meeting in Chicago, is reported by B.U.P. to have complained of "marked deterioration" in medical teaching in most overseas countries since 1935. With European countries particularly in mind, the federation resolved that no candidate should be admitted for examination who graduated after that year; all who graduated before then will be obliged to meet the requirements of the board of medical examiners in the State where they are seeking a licence. Dr. Creighton Barker told the meeting that 48% of the graduates of foreign medical schools examined between 1930 and 1947 had failed to pass. In a further resolution the federation deplored the practice of granting government financial assistance to ex-Servicemen taking medical courses in foreign schools, and asked that no more candidates be allowed to register in these schools.

Diary of the Week

MARCH 6 TO 12

Monday, 7th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. F. S. Gorrill: Anatomy and Physiology of Bone—part I. (Arnott demonstration.)
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
9 P.M. Dr. Horace Evans: Richard Bright, Before and After. (Last Lettsomian lecture.)
HUNTERIAN SOCIETY
8.30 P.M. (Mansion House, E.C.4.) Sir Henecage Ogilvie: Personal Experiences. (Hunterian oration.) *Amended notice.*
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.15 P.M. Dr. A. C. Roxburgh: Dermatology as it Concerns the Ear, Nose, and Throat.

Tuesday, 8th

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: The Dermatophytes.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
9.30 A.M. Mr. Myles Formby: Non-operative Treatment of Maxillary Sinusitis.
CHELSEA CLINICAL SOCIETY
7.30 P.M. (South Kensington Hotel, 47, Queen's Gate Terrace, S.W.7.) Mr. Wylie McKissock, Dr. Desmond Curran: Prefrontal Leucotomy.

Wednesday, 9th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. P. H. Mitchiner: Anatomy of the Tongue and its Relation to Surgery. (Arnott demonstration.)

Thursday, 10th

ROYAL SOCIETY, Burlington House, Piccadilly, W.1
4.30 P.M. Sir Charles Harington, F.R.S.: Work of the National Institute for Medical Research.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. L. Forman: Bullous Eruptions.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Neurology lecture-demonstration.
UNIVERSITY OF LIVERPOOL
5 P.M. (Arts Theatre.) Prof. E. D. Adrian, O.M., F.R.S.: Sensory Integration. (Sherrington lecture.)

Friday, 11th

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. Parry Brown: General Anæsthesia for Surgery of the Heart.

Institute of Almoners

Dr. John B. Grant, European director of the Rockefeller Foundation's international health division, will speak at the institute's annual meeting, which is to be held at the Central Hall, Westminster, on Friday, March 25, at 6.30 P.M.

U.S. Investigation of Alcoholism Treatment

A committee of eight, under the chairmanship of Prof. Edwin Zabriskie, of Columbia University, has, according to B.U.P., been set up to investigate the use of tetraethylthiuramdisulphide in the treatment of alcoholism. This drug ('Antabuse') was the subject of two articles in our issue of Dec. 25.

Sir Alexander Fleming, F.R.C.P., F.R.S., is to receive the freedom of the borough of Chelsea on March 16.

Dr. A Piney has been elected a foreign member of the Swiss Hæmatological Society, and has been appointed a member of the editorial board of *Acta Hæmatologica.*

A booklet on *Safety Measures in Chemical Laboratories* which was originally prepared for the guidance of newcomers to the Chemical Research Laboratory, Teddington, is now obtainable from H.M. Stationery Office, price 6*d.*

A Guide to Pacific Island Dietaries has been compiled by Dr. J. C. R. Buchanan, inspector-general, South Pacific Health Service. This book, issued from the service's headquarters office, Suva, Fiji, is addressed primarily to students and graduates of the Central Medical School, Suva.

Appointments

BUCKLEY, P. S., B.M., B.SC. Oxfd, M.R.C.P.: visiting neurologist, Seamen's Hospital, Tilbury.
JAMIESON, R. F., M.B. Glasg., D.O.M.S.: visiting ophthalmic surgeon, Central Clinic, Barking.
KING, R. A., M.B.E., M.B. Lond., F.R.C.S.: orthopædic surgeon, Oldchurch Hospital.
KLEIN, MIKLOS, M.D. Pecs, D.O.M.S.: ophthalmic consultant, Whipps Cross Hospital.
LASK, SAMUEL, M.D. Leeds, M.R.C.O.G.: assistant specialist (obstetrics and gynæcology), St. Andrew's Hospital, Bow.
MANDERSON, W. G., M.B. Glasg.: deputy resident physician (fevers), Ham Green Infectious Disease Hospital and Sanatorium, Bristol.
NELSON-JONES, ARCHIBALD, M.D. Lond., M.R.C.P.: medical examiner to the North-East Metropolitan Regional Hospital Board.
NEUSTATTER, W. L., M.D., B.SC. Lond., M.R.C.P.: visiting psychiatrist, Hertford County Hospital.
O'FARRELL, A. W. J., M.B. N.U.I., D.P.H.: radiotherapist, United Cardiff Hospitals.
SIMS, H. C., M.D., PH.D. Cologne, D.M.R.: radiotherapist, Oldchurch Hospital.
STEWART, J. M., M.B. Lond., D.M.R.D.: radiologist, Oldchurch Hospital.
URQUHART, H. M., M.B. Edin., F.R.C.S.E.: ear, nose, and throat surgeon, Northern Regional Hospital Board.
WATERFALL, W. B., B.A., M.B. Camb., F.R.C.S.: surgeon, Prince of Wales's Hospital, Plymouth.

Fulham Hospital, London:

BARRITT, D. W., M.B. Lond., M.R.C.P.: senior medical registrar.
BOND, S. A., M.B. Glasg., M.R.C.O.G.: senior registrar (gynæcological).
GRAEME, M. L., M.B. Camb.: junior surgical registrar.
OATWAY, A. W. N., M.A., M.B. Camb.: junior medical registrar.
TEMPLE, J. L., M.B. Lond.: senior surgical registrar.
VYSE, J. A., M.B.: casualty registrar.

Colonial Service:

BAXTER, G. F., O.B.E., M.R.C.S.: senior M.O., Jamaica.
BELEJ, JAN, M.D. Lwow: temporary M.O.H., Gold Coast.
BOURKE, P. J., L.R.C.P.E.: senior M.O., Nyasaland.
BRADBURY, ERIC, B.CHIR. Camb., D.T.M., D.T.H.: senior M.O.H., Sierra Leone.
BRERETON, A. B., M.B. Edin., D.M.R.E.: radiologist, Gold Coast.
BYRNE, J. A., M.B. Belf.: M.O., Gold Coast.
CHWAT, L. J. L., M.D. Warsaw: senior malariologist, Nigeria.
HARRY, G. V., M.B. Edin.: senior surgeon, Jamaica.
LATHAM, C. N., M.B. Birm., D.T.M. & H.: senior M.O., Nigeria.
MCLAREN, D. W., M.B. Durh., D.T.M.: senior M.O., Nigeria.
MCLELLAND, W., M.B. Glasg., D.T.M. & H.: senior M.O., Nigeria.
MCLETCHIE, J. I., M.B. Glasg., D.T.M. & H.: senior M.O., Nigeria.
MOLESWORTH, B. D., M.B. Camb.: medical superintendent, Loper Settlement, Federation of Malaya.
MURRAY, C. P., M.B. Aberd.: senior M.O., Nigeria.
PHILLIPPS, W. R., M.B. N.Z., D.T.M. & H.: surgical specialist, Gold Coast.
REECE, A. A., M.D.: M.O. grade B, Trinidad.
STEVENS, C. E. E., M.B. Belf., F.R.C.S.E.: medical superintendent, Cunningham Hospital, Leeward Islands.
STRAHAN, J. H., M.B., B.SC. Belf., D.P.H., D.T.M. & H.: professor of social medicine and hygiene, Singapore.
WALCZAK, Z. P., M.B. Polish School of Medicine: supernumerary M.O., Leeward Islands.
WANDS, HUGH, M.B.E., M.B. Glasg.: deputy director of medical services, North Borneo.
WATT, GEORGE, M.B.E., M.B. Edin., D.T.M. & H.: asst. director of medical services, Gold Coast.

Digitized by Google

HISTORICAL BUILDING
DES MOINES, IOWA

VALUE OF SYSTEMIC PENICILLIN IN FINGER-PULP INFECTIONS

A CONTROLLED TRIAL OF 169 CASES

STEWART H. HARRISON
F.R.C.S.
SURGEON

ELIZABETH TOPLEY
M.B. Lond.

J. LENNARD-JONES
B.A. Camb.

MEMBERS OF M.R.C. INDUSTRIAL MEDICINE RESEARCH UNIT
BIRMINGHAM ACCIDENT HOSPITAL

THE serious economic loss to industry from hand sepsis is well recognised. For example, in a large engineering factory in Birmingham 25% of compensation cases had septic hands (J. P. Bull, personal communication, 1948). It follows that any reduction in healing-time, or a quicker return to full function, should be of material advantage both to patients and to industry. The question obviously arises whether penicillin can contribute to these improvements.

Finger-pulp infections appeared to be suitable clinical material for investigating the value of systemic penicillin, because some 90% of them are due to penicillin-sensitive *Staphylococcus aureus*; because the surgical pathology can be defined at operation; and because the lesion, while being one of the commonest forms of sepsis taking more than a fortnight to heal, is mild enough for there to be no moral obligation to give penicillin as a routine, until its value is fully proved.

By a "finger-pulp infection" we mean that the finger shows clinical signs of inflammation in the region of the pulp tissue—i.e., the firm fibrofatty pad between the terminal phalanx and the skin on the volar surface. It is possible to subdivide these cases into many clinical subgroups. We will emphasise only the subdivision into the true pulp infection involving the subcutaneous pulp tissue, and the more superficial abscesses termed by Pilcher "intracutaneous" (Pilcher et al. 1948).

In investigating these finger-pulp infections our primary aim was, by a carefully controlled trial, to demonstrate the effect of systemic penicillin. One series of patients received systemic penicillin while another series received none. Care was taken that these two series were parallel random samples of the same hospital population. Each patient was first examined by one of us, asked if he could come into hospital for 5 days, and only if he agreed was allocated to one or other series by reference to a previously prepared list. The clinical findings on admission (table I) suggest that the two series were virtually random.

Given two comparable series of patients on admission, care had to be taken that the patients in both series received identical treatment in all respects other than systemic penicillin. All details, including criteria for operation, were therefore prescribed in writing and applied to all patients. There were, however, times when the routine surgical treatment was changed in an attempt to improve it. The major alterations are shown in table II, which divides the patients into four treatment groups, the first three inpatient groups following consecutively.

A few cases had to be excluded from the series. For inpatients the only reasons were failure to give the prescribed penicillin—e.g., if the patient had to be discharged before the course was finished—or failure to stay in hospital for 5 days. In the outpatient series no case was excluded, but this series was less satisfactory for demonstrating any effect due to penicillin because of the irregular attendance for injections.

The postoperative data were collected by a personal follow-up of every patient, care being taken to avoid any bias between penicillin and no-penicillin cases either in frequency of attendance (table I) or in clinical examination. The clinical data can be used in various ways. They can be used to learn the value of systemic penicillin. They can be used, if extreme care is taken to avoid the pitfalls, to compare the results of different surgical treatments, particularly those of a minimal incision into the area of greatest tenderness, with those of the large lateral J-shaped incision. Another question is whether, by giving penicillin, incision can be avoided altogether. The evidence on these points will be presented as follows:

(1) The effect of systemic penicillin on the postoperative course.
(2) A comparison of lateral J-shaped and minimal incision.
(3) The results of delaying operation in patients receiving penicillin.
(4) A new technicque for the measurement of swelling of an infected finger.

Effect of Systemic Penicillin on Postoperative Course

The economic effect could have been measured in terms of days off work and end-results. The difficulties were that days off work are affected by many issues other than clinical condition, and end-results cannot be measured quantitatively. Healing-time and complication-rate are measurable and closely associated both with these economic aspects and with other clinical findings. The following description concentrates on the reduced healing-time and reduced complication-rate produced by systemic penicillin. Emphasis is not laid on the other recorded results (often not statistically different in their incidence in the two series) though, for every item tested, the penicillin series fared better than the no-penicillin series—a difference largely contributed by the lower incidence of complicated cases.

Healing-time

By "healed" we mean that the skin was seen on inspection to be epithelised, and that no scab was present at subsequent visits. The healing-time after incision or blister-cutting was calculated from our records taken

TABLE I—EVIDENCE OF COMPARABILITY OF "SYSTEMIC PENICILLIN" AND "NO SYSTEMIC PENICILLIN" SERIES

—	Systemic penicillin	No systemic penicillin	Whether difference significant by χ^2 or "t" test
Total no. of patients	83	86	..
Mean age (years)	30·3	28·8	No
Males/females	45/38	56/30	No*
No. with history of accident	48	51	No
Mean interval from accident to first symptom (days)	4·0	3·9	No
Mean interval from symptom to admission (days)	3·7	4·1	No*
No. with thumb affected	29	31	No
No. with pus visible on admission	48	42	No
No. with tenderness on admission extending to middle phalanx	13	12	No
No. incised on day of admission	42	50	No
Mean no. of days to final follow-up	109	110	No
Mean no. of attendances	7·7	7·5	No

* Separate analysis of the surgical treatment groups (groups 1, 2, 3, and 4 in table II) revealed the following differences between the systemic penicillin and no systemic penicillin series:

(1) Among cases treated in hospital (groups 1, 2, and 3) there was a significantly higher proportion of females in the systemic penicillin series (penicillin 12/51, no penicillin 3/53, χ^2 5·36 $P < 0·05$).
(2) Of the outpatients (group 4) the systemic penicillin series had a significantly shorter average history (penicillin 3·2 days, no penicillin 4·3 days).

The results have been reviewed to see whether this distribution could have favoured the patients receiving systemic penicillin. There is no evidence of this. For example, the significant advantages of systemic penicillin over no systemic penicillin persists if either all female inpatients or all outpatients are excluded.

Digitized by Google

at special weekly clinics. It was the average of "days to healed" and "days to last known to be unhealed." The healing-time of patients receiving no operation (penicillin 6, controls 4) were counted as 0 days.

Table II shows that for each treatment group the patients receiving systemic penicillin had the shorter mean healing-time. Taking the totals, systemic penicillin had an average of 13·8 days, and no systemic penicillin 20·1 days. The difference is 6·3 days—a difference which when submitted to "t" testing is highly significant ($P < 0.02$). The two series are strictly comparable. The difference can therefore be ascribed with confidence to the systemic penicillin. The difference persists if all anomalous cases are excluded, such as intracutaneous as distinct from true pulp infections, or lesions not due to *Staph. aureus*. As table II shows, the difference is still significant if one confines attention to the treatment groups in which the controls received local penicillin as a routine and systemic penicillin for complications.

Postoperative Complications

These complications are shown in table III. Brief reference must be made to anomalous cases in the systemic penicillin series. There were 2 patients, both treated by the lateral J-shaped incision, whose fingers were almost, but not quite, healed at one visit and yet were found 1–2 weeks later to have developed a pocket of pus. Such a finding was never noted in the control lateral-J cases or after any minimal incision. Another anomalous finding was a single penicillin case in which the finger showed local radiographic changes in the absence of any other complication. Of the 2 systemic penicillin cases in the unsatisfactory end-result category one was admitted with a sequestrated terminal phalanx, while in the other the finger was already scarred from an old pulp infection and the current lesion was not due to *Staph. aureus*.

With these exceptions (all included in table III) the complications fell into a well-defined single syndrome, always starting with the appearance of pus and slough. Of the control patients, 41 showed pus and slough, of whom 9 showed other signs of secondary inflammation, such as considerable swelling of the finger or extension of the inflammation. The 15 local radiographic changes were in these fingers and in some fingers showing pus and slough only. The very unsatisfactory end-results were almost all in fingers which had shown secondary inflammation. Each aspect of the complication syndrome had a lower incidince in the penicillin than in the no-penicillin series. The difference is statistically significant where the numbers of cases are large enough for statistical analysis.

TABLE III—POSTOPERATIVE COMPLICATIONS WITH AND WITHOUT SYSTEMIC PENICILLIN

Complication	Systemic penicillin (83 patients)	No systemic penicillin (86 patients)	Significance by χ^2 testing
Pus or slough ..	23	41	χ^2 = 6·29 P = <0·02 S
Local radiographic rarefaction	3	15	χ^2 = 7·09 P = <0·01 S
Early secondary inflammation (1st 14 postoperative days)	1	9	χ^2 = 4·90 P = <0·05 S
Late secondary inflammation (after 1st 14 postoperative days)	2	0	..
End-result: severely tender or scarred finger	2	6	..

S = significant.

The economic importance of these complications lies in their close association with delayed healing and the risk of ending with a scarred or tender finger.

Bacteriology

Swabs were taken at operation and at most subsequent dressings. The results (table IV) show that systemic penicillin significantly reduced the incidence of *Staph. aureus* in the first postoperative swab, a result not produced by local penicillin alone. This supports the obvious hypothesis that the systemic penicillin is producing its clinical effect by its action on the pathogenic organisms which probably initiate and spread the disease. Penicillin-resistant *Staph. aureus* (resistant to 0·1 unit per ml.), penicillinase-producing *Staph. aureus*, and any pathogen other than *Staph. aureus* were all so rare that we can offer no useful information on the value of penicillin in lesions produced by these organisms.

Comparison of Lateral J-shaped and Minimal Incisions

Effect on Postoperative Course

We must now consider the improvement in the treatment groups as the investigation proceeded.

Table II shows that in the control series the mean healing-time fell from 35·3 to 12·0 days. It requires detailed knowledge of these groups to give possible reasons for this fall. The reason for the difference between groups 1 and 2 might be the introduction of local penicillin for all patients. The case for local penicillin in addition to systemic penicillin rests on the fact that systemic peni-

TABLE II—MEAN HEALING-TIMES FOR DIFFERENT TREATMENTS WITH AND WITHOUT SYSTEMIC PENICILLIN

Group	Treatment						Results					
	Systemic penicillin (if any)			Other treatment			Systemic pen.		No syst. pen.		Diff.	Standard error of difference
	Units initial	Units daily (for 5 days)	Frequency of injections	Local penicillin	Op.*	Hosp.†	No. of patients	Mean healing-time (days)	No. of patients	Mean healing-time (days)		
1	100,000	100,000–160,000	3-hrly	0	J	In	15	20·00	13	35·31	15·31	10·60
2	500,000	1,000,000	3-hrly	+	J	In	10	17·70	11	27·00	9·30	5·16
3	500,000	1,000,000	3-hrly	+	MI	In	26	13·96	29	19·76	5·80	3·71
4	500,000	1,000,000	b.d.	+	MI	Out	32	9·53	33	12·03	2·50	1·78
Total	..	..	..	..	..	..	83	13·80	86	20·07	6·27‡	2·49
2, 3, 4	500,000	1,000,000	..	+	..	In/Out	68	12·43	73	17·36	4·93§	2·05

* Op. J = lateral J-shaped incision; MI = minimal incision. † Hosp. In = Inpatient; Out = Outpatient.
‡ $t = 2·52$; $P = <0·02$–significant. § $t = 2·40$; $P = <0·02$–significant.

Digitized by Google

cillin does not reduce *Staph. aureus* skin carriage (Moss et al. 1948). The local penicillin is therefore theoretically required to reduce the risk of added infection of the wound from the pus-contaminated skin. The difference between groups 1 and 2 might also be due to the introduction of systemic penicillin for complications in control patients, and the increased dosage of systemic penicillin in the penicillin series. It is impossible to estimate the effect of these changes. They were introduced to compare the value of optimum systemic penicillin therapy with penicillin used only locally or for complications. The reason for the difference between groups 3 and 4 is probably that the outpatients included a higher proportion of intracutaneous as against true pulp infections.

The difference between groups 2 and 3 lies in the operation done. Though it is impossible to be certain that these groups are comparable in all other respects, the significant improvement in postoperative results can probably be ascribed to the adoption of the minimal incision technique.

The mean healing-time is lower in the minimal incision group (table II) but this is not statistically significant because of the small numbers of cases. There are, however, significantly fewer cases (table V) which take 28 days or more to heal in the lateral J-shaped incision group—a point of some practical importance.

The cases which received no systemic penicillin showed a lower complication-rate with minimal incision (table VI). The statistically significant difference was in the incidence of pus and slough. Among patients receiving systemic penicillin these differences are not so evident, but the incidence of acute inflammation and radiographic rarefaction was again slightly lower with minimal incision than with lateral J-shaped incision.

The minimal incision scar was almost always subjectively much more satisfactory than the lateral J-shaped scar. In most of the fingers which had the minimal incision there was no palpable abnormality of any kind, and all that could be seen on close inspection was a fine linear loss of skin markings about $^1/_4$ in. or less in length.

In the present state of knowledge we consider it unjustifiable to continue the use of the lateral J-shaped incision. Our best results were obtained with systemic penicillin plus minimal incision. The technical details of the minimal incision are therefore worth recording in some detail.

TABLE IV—ISOLATION OF *Staph. aureus* FROM FIRST POSTOPERATIVE SWAB * WITH AND WITHOUT SYSTEMIC PENICILLIN †

—	No. of patients				Significance by χ^2 testing
	With swab ++ ‡	With swab + ‡	With swab O ‡	Total	
Local penicillin— at operation	24	5	4	33	$\chi^2 = 13{\cdot}27$
plus systemic penicillin 3-hourly	7	9	11	27	$P = <0{\cdot}01$
Local penicillin— at operation	18	5	4	27	$\chi^2 = 13{\cdot}75$
plus systemic penicillin prescribed twice daily	4	13	8	25	$P = <0{\cdot}01$
Total local penicillin— at operation	42	10	8	60	$\chi^2 = 28{\cdot}88$
plus systemic penicillin	11	22	19	52	$P = <0{\cdot}001$

* Swab usually taken 3 days after operation.

† Systemic penicillin—1,000,000 units daily, usually for 3–5 days before postoperative swab.

‡ ++, *Staph. aureus* colonies extending beyond area of direct spread on penicillinase blood-agar plate.
+, *Staph. aureus* colonies either confined to area of direct spread or only present on subculture of broth culture.
O, no *Staph. aureus* isolated even by anaerobic broth subculture method.

χ^2 testing of comparable groups shows that significantly fewer *Staph. aureus* colonies were isolated from patients receiving systemic penicillin.

TABLE V—COMPARISON OF HEALING-TIMES WITH LATERAL J-SHAPED AND MINIMAL INCISIONS

—	Lateral J-shaped incision (group 2)*	Minimal incision (group 3)*
Fingers healed in less than 28 days	12 (57%)	46 (84%)
Fingers healed in 28 days or more	9	9
Total	21	55

* See table II for further details of these groups.
$\chi^2 = 4{\cdot}54$. $P = <0{\cdot}05$.—significant.

TABLE VI—NUMBER OF PATIENTS WHOSE FINGERS SHOWED POSTOPERATIVE COMPLICATIONS WITH LATERAL J-SHAPED AND MINIMAL INCISIONS

—	Systemic penicillin		No systemic penicillin	
	Lateral J-shaped incision (10 patients)	Minimal incision (26 patients)	Lateral J-shaped incision (11 patients)	Minimal incision (29 patients)
Pus or slough	3 (30%)	9 (35%)	10 (91%)	14 S (48%)
Local radiographic rarefaction	1 (10%)	1 (4%)	4 (36%)	5 (17%)
Acute inflammation	2 (20%)	0	3 (27%)	3 (10%)

S = significant for no systemic penicillin. $\chi^2 = 4{\cdot}38$. $P = <0{\cdot}05$.

Minimal Incision and Atraumatic Technique

Whatever support the minimal incision may or may not receive from statistical information, it seems to us to be of first importance clinically. It was evolved by one of us (S. H. H.) from a close study of pulp infections at operation.

The lateral J-shaped incision divides all the fibrous septæ of the finger but does not necessarily prevent the pus from discharging through the pulp. All too often a sinus to the pulp is formed before the patient comes to operation, and the lateral J-shaped incision will not reverse the flow. The extensive incision must contaminate with bacteria previously uninfected sites.

TABLE VII—FINAL TREATMENT OF FINGERS NOT INCISED ON DAY OF ADMISSION, SHOWING THAT A FINGER SWOLLEN MORE THAN 10% USUALLY REQUIRED INCISION

Surgical treatment	Systemic penicillin		No systemic penicillin	Total (S)
	Deliberate delay	Early operation	Early operation	
Finger volume 10% or less on admission:				
Incision	1	5	4	10
No operation, or blister cut only	4	3	2	9
Finger volume more than 10% on admission:				
Incision	6	7	10	23
No operation, or blister cut only	1	3*	0	4
Total:				
Incision	7	12	14	33
No operation, or blister cut only	5	6	2	13

* All of these 3 patients had fingers swollen only very slightly more than 10%—i.e., 11%, 12%, and 12%.
S = significant. $\chi^2 = 4{\cdot}33$. $P = <0{\cdot}05$.

Digitized by Google

TABLE VIII—SHOWING THAT PUS IS USUALLY PRESENT IN FINGER SWOLLEN MORE THAN 10%

Finger-volume on day of operation	Operation finding	
	Pus in pulp	No pus or intracuticular pus only
Less than 10%	2	7
More than 10%	45	7

$\chi^2 = 14{\cdot}44$. P = <0·001 significant.

In the minimal incision emphasis is laid on the removal of keratinised skin overlying the sinus and area of greatest tenderness. By this procedure the pathology is sharply defined and the full extent of the sinus exposed. Pocketing between the keratin layer and the true skin is avoided, and penicillin applied locally is allowed full access to that part of the skin which might permit the overflow of organisms into the wound. If the sinus is large enough, no incision is required. In about half the cases a stab incision is necessary. This is made through the minute sinus, or through the point of purplish discoloration which precedes the formation of a sinus, or, in the absence of any visual sign, through the predetermined area of greatest tenderness. In no case have we failed to locate an abscess on the first incision. The incision lies parallel to Langer's lines and is never more than a stab with the point of a fine Bard Parker no. 10 blade. The abscess is opened and its extent explored. Fine forceps and scissors are used to excise the slough and unhealthy subcutaneous tissue.

The area of skin surrounding the sinus has an impoverished blood-supply, and the success of the operation depends on a rigid adherence to atraumatic technique. It should never be necessary to grasp the skin edges, use retractors, or pack the wound.

Great care and some experience are required to make sure that the resulting cavity is clean and free from at least visible dead tissue. General anæsthesia, a pneumatic tourniquet, and a liberal stock of patience are all essential. Finally, the surgeon himself should apply the bandage firmly and with care. Even pressure along the digit and a bandage that does not slip are by no means unimportant parts of the operation.

It has become our practice to do dressings on the third day after operation and subsequently at 7-day intervals. This may have clinical advantages, for the infrequency of the dressings will not only lower the risk of added infection but also will benefit the economic position of both the patient and the hospital dressing-clinics. The principles of elevation and immobilisation have been maintained in so far as the finger has been efficiently bandaged and the patient kept in bed for 5 days.

TABLE IX—CLINICAL PROGRESS OF FINGERS NOT INCISED ON THE DAY OF ADMISSION, WITH AND WITHOUT SYSTEMIC PENICILLIN

A. CHANGE IN PHYSICAL SIGNS DURING FIRST 24 HR. IN HOSPITAL

Physical sign	Systemic penicillin (No. of patients)			No systemic penicillin (No. of patients)		
	Less or same	More	Totals	Less or same	More	Totals
Area of subcuticular pus ..	14	13	27	13	10	23
Degree of apparent swelling	12	10	22	9	13	22
Area of tenderness ..	22	4	26	10	13	23S

B. OPERATION FINDINGS IN FINGERS INCISED ON 2ND DAY IN HOSPITAL

Operation finding	Systemic penicillin (No. of patients)			No systemic penicillin (No. of patients)		
	+	O	Totals	+	O	Totals
Pulp extensively involved ..	5	14	19	2	12	14
Pus in contact with periosteum	7	11	18	3	11	14
Pus in contact with tendon sheath	2	16	18	2	12	14
Staph. aureus isolated	18	1	19	12	1	13

S = significant. $\chi^2 = 7{\cdot}38$. P = <0·01.

A shows that with systemic penicillin the area of tenderness often did not extend. B shows no effect of systemic penicillin.

TABLE X—COMPARISON OF FINGER-VOLUME ON ADMISSION WITH MEASUREMENT 24 HOURS LATER, SHOWING THAT THE AFFECTED FINGER CONTINUES TO SWELL DURING THE FIRST DAY OF TREATMENT WITH SYSTEMIC PENICILLIN

Patients receiving systemic penicillin	Change in volume of affected finger (c.cm.)	Change in volume of corresponding unaffected finger (c.cm.)
1	+0·03	−0·19
2	+0·09	−0·05
3	+0·26	−0·20
4	+0·04	+0·14
5	+0·09	−0·17
6	+0·10	+0·05
7	+0·13	−0·02
8	+0·13	..
9	+0·38	−0·16
10	+0·12	−0·15
11	−0·02	−0·01
Mean	+0·123	−0·076
Standard error of mean	0·1661	0·0058
Probability that true mean is zero	0·01	0·1
Change in volume..	Significant	Not significant

Results of Delaying Operation

Day-to-day records are available on the clinical progress of 77 patients whose fingers were not incised on admission, and on a further 16 in whom operation was deliberately delayed. These results indicate:

(1) Which clinical cases may not require incision at all.

(2) How penicillin may alter the preoperative course and affect the need for incision.

(3) How deliberate delay of operation may affect the postoperative findings.

The daily observations included the results of a special fluid-displacement technique for measuring the finger-volume as described below. Volumetric measurements were made on the affected finger and another finger, usually the corresponding one of the opposite hand. The expected normal of the affected finger could be calculated by reference to a table compiled from measurements made on many normal people. The swelling was then expressed as a percentage increase over the expected normal. Clinically, a swelling of less than 10% is barely perceptible; as a rule a swelling of more than 10% is associated with obscured skin markings on the dorsum of the finger, visible swelling and some tenseness of the pulp, and enough stiffness to limit movement of the terminal interphalangeal joint.

Table VII shows that many fingers swollen less than 10% above the expected normal never required incision. It follows that there is a case for delaying incision, at least if no pus is visible (table VIII). In contrast, the finger swollen more than 12% almost invariably contained pus and almost invariably required operation. In the definitely swollen finger it is therefore unlikely that incision will be avoided, however long the delay.

Digitized by Google

Our knowledge of how penicillin alters the prognosis of the unswollen finger is limited by the small number of cases. As can be seen from table VII, in the fingers swollen less than 10% on admission incision was less often necessary in the penicillin than in the control series, but the difference is not statistically significant. For fingers swollen more than 10% we have shown that penicillin usually does not avoid the necessity of incision. Does it in any way alter the clinical syndrome? Table IX shows that during the first 24 hours after admission systemic penicillin did not alter the findings for apparent swelling, area of subcuticular pus, operation findings of extent of pulp involved, whether or not bone was exposed, or presence of *Staph. aureus* in pus. Finger-volume measurements showed (table X) that there was a significant increase in finger volume during the first 24 hours of penicillin. In contrast to these negative findings, systemic penicillin did seem to limit the extension of the area of tenderness.

The data on the 16 patients in whom operation was deliberately delayed helped to show, as described above, that in the presence of significant swelling penicillin only rarely will avoid the necessity of operation. They also provide evidence that delay in incision of the swollen finger may do harm. The postoperative findings in these 16 cases can be compared with the postoperative findings in the parallel penicillin and no-penicillin patients receiving early operation—these three series being random samples of the same hospital population. The "penicillin plus delay" series had a longer mean healing-time and a higher complication-rate than the "penicillin, early operation" series (table XI). Since the unsatisfactory results were all in fingers swollen more than 20% on admission, it was considered clinically unjustifiable to delay incision beyond this point, and this investigation was therefore discontinued.

TABLE XI—RESULTS OF DELIBERATELY DELAYING OPERATION. COMPARISON OF THREE GROUPS OF PATIENTS WHICH WERE PARALLEL RANDOM SAMPLES OF THE SAME HOSPITAL POPULATION

Result	Systemic penicillin		No systemic penicillin
	Early operation (15 patients)	Delayed operation (16 patients)	Early operation (15 patients)
Tendon-sheath infection	0	1	0
No operation	0	4	1
Mean healing-time (all fingers)	14·8	19·9	26·9*
Standard error of mean	1·84	4·58	6·16
Mean healing-time (incised fingers)	14·8	26·5	28·7
Postoperative pus and slough	5	6	10
Local radiographic rarefaction	0	4	5
Acute inflammation ..	0	0	3
End-result (severe scar or tenderness)	1†	1	2

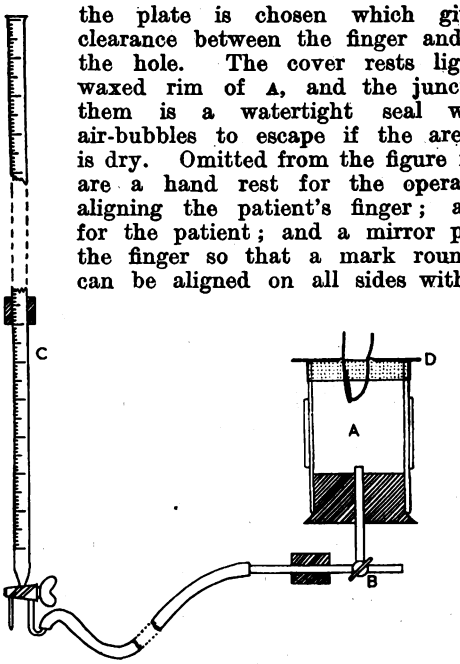
* High mean due to one patient whose finger took 96 days to heal.
† See text for reasons for not considering this a penicillin failure.

Measurement of Swelling of an Infected Finger

(J. E. LENNARD-JONES)

Measurement of Finger-volume

The essentials of the water-displacement apparatus used are shown in the figure. The particular feature of the apparatus is the detachable 'Perspex' cover-plate, D. A series of these plates is available, each of which has a different size of central hole, and for each measurement the plate is chosen which gives a small clearance between the finger and the side of the hole. The cover rests lightly on the waxed rim of A, and the junction between them is a watertight seal which allows air-bubbles to escape if the area of contact is dry. Omitted from the figure for simplicity are a hand rest for the operator, used in aligning the patient's finger; an arm rest for the patient; and a mirror placed behind the finger so that a mark round the finger can be aligned on all sides with the surface of the plate.



Apparatus for measuring finger volume: A, glass vessel with upper part waxed; B, 3-way tap; C, 50 c.cm. burette graduated in 0·05 c.cm.; D, detachable perspex cover-plate.

A line is carefully marked round the finger, with the volar and lateral creases of the distal interphalangeal joint as points of reference. The finger is inserted through the hole in the plate, gripped lightly between the index finger and thumb of the operator, and aligned so that the mark is everywhere at the level of the surface of the plate. By turning tap B, water is run into A until the surface is level with the top of the plate in the narrow space between the finger and the side of the hole. The finger is withdrawn, the hole in the plate is covered with a lightly waxed microscope slide, and water is run into A until it is in contact with the waxed slide over the hole. The volume of water required corresponds to the volume of the phalanx.

All observations are recorded as the mean of three successive measurements. The standard deviation of the difference between two such means lies between 0·18 c.cm. (2·4%) for the thumb and 0·12 c.cm. (3·6%) for the little finger (values derived from observations made on all the digits of 13 people). When one mark is used two means may be compared with about the same accuracy whether they are obtained on the same or different days. Normal circulatory changes in the finger produce small changes in finger volume and may be ignored.

Estimation of Amount of Swelling

The results obtained from measuring all the digits of 13 normal people are summarised below. It will be seen that the size of one finger can be estimated with an accuracy of 12% ($P = 0.05$) from the size of another finger. The magnitude of this error is due to biological variation and to the difficulty of obtaining an anatomically constant mark rather than to instrumental errors. The results also show that in right-handed people the digits of the right hand are larger than those on the left, at least for the most used digits.

The size of a normal finger can be estimated from the size of other normal fingers in two ways:

(1) From the corresponding finger on the opposite hand. The figures given below show the correction which must be applied in a right-handed person owing to the lack of symmetry between the two hands.

(2) From the middle finger on the same hand. The sizes of the three fingers, but not the thumb, each bear a fairly constant ratio to the size of middle finger.

Digitized by Google

The figures obtained were as follows:

Method	Digit to be estimated I	II	III	IV	V
(1) The size of the right digit expressed as a percentage of the size of the left in right-handed people	106 (± 4)	108 (±5)	106 (±4)	104 (±5)	103 (±6)
(2) The size of each digit expressed as a percentage of the size of the middle finger in the same hand	162* (±18)	92 (±6)	100	88 (±4)	68 (±5)

The standard deviation of each value is given in parentheses. Apart from the one value for the thumb marked * the standard deviation does not exceed 6%, and therefore any difference between the observed volume and the estimated volume of a finger exceeding 12% may be considered significantly different from normal ($P = 0.05$).

Discussion

The results of previous attempts to demonstrate the value of systemic penicillin in finger-pulp infections have shown that the effect is not dramatic and can easily be obscured by other factors. d'Abreu's successful 7 pulp infections and paronychia were compared with 135 earlier cases not receiving penicillin (d'Abreu et al. 1947). Loudon et al. (1948) had no controls but compared their results with other published series in which local penicillin had been evaluated (Florey and Williams 1944, Curr 1945). Webster (1947) has, however, clearly demonstrated the uselessness of comparing the results of treatment carried out at different times, by showing that his patients treated without penicillin fared very much better than earlier cases similarly treated. Like us, he found an improvement in results as the investigation continued; but, since his penicillin-treated cases preceded the no-penicillin cases, the implication was that penicillin was not of much value. Bolton et al. (1947) treated 69 simple felons, alternate cases having penicillin 100,000 units daily. They found "no significant difference in morbidity time or development of complications in the two classes." The detailed figures are not published.

The present investigation was designed to assess by a controlled trial the value of systemic penicillin to patients receiving the optimal associated treatment. Comparing "systemic penicillin" with "no systemic penicillin" we have found that the patients receiving systemic penicillin showed a significantly reduced healing-time and a significantly reduced complication-rate—not dramatic in extent but, we suggest, very well worth the time, cost, and trauma of the injections. The use of local penicillin as a routine and systemic penicillin for complications was not in itself adequate. We therefore consider that there is a case for the routine administration of systemic penicillin in all genuine cases of subcutaneous finger-pulp infections.

We have not enough cases to say whether systemic penicillin was valuable in the intracutaneous infections. Since it is impossible always to differentiate the two before operation, there is something to be said for a single preoperative injection of penicillin followed by a further course if the pulp tissue is found to be involved.

The investigation was not designed to do more than prove whether or not systemic penicillin was valuable, but the experience gained from the present trial inevitably led to other hypotheses. Review of the literature, especially the correspondence in these columns after the provocative article of Pilcher et al. (1948), shows that conflicting views are held on surgical treatment.

We have defined the atraumatic technique of minimal incision through the area of greatest tenderness. This should be applicable to the surgery of hand sepsis in general. For the finger-pulp infection, we compared our results by this method with those for the lateral J-shaped incision. Though we have not shown by a controlled trial that the minimal incision is superior, all the evidence points this way. We consider it clinically unjustifiable to continue the use of the lateral J-shaped incision, except possibly in a controlled trial designed to assess effectively its value.

Pilcher discusses theoretically when to incise a finger (Pilcher et al. 1948). Our finding that a finger swollen less than 10% often never required incision adds support to his practice of delaying operation in the extremely early cases. Our very unsatisfactory results of delaying incision once the finger was swollen more than 20% suggests that the hospital case that will benefit from delay is not common.

We have no evidence on the optimal dosage or frequency of administration of systemic penicillin; those we used are shown in table II, and the bacteriological results in table IV.

Further trials are necessary in many hospitals and communities, particularly on the best method of out-patient administration of penicillin, on the value of penicillin as an aid to avoiding incision of the very early pulp infection, and on the best time for incision. Carefully controlled trials of different parallel treatments, using necessity of incision, healing-time, and complication-rate as criteria, should produce many useful answers.

Summary

In a controlled trial of 169 finger-pulp infections systemic penicillin reduced the mean healing-time by 6 days and reduced the complication-rate. Such an improvement should be of importance to industry and to the patient. It is not obtained with local penicillin.

The associated treatment was altered as the investigation continued. It is suggested that the improvements in results were in part due to the adoption of a minimal incision over the area of greatest tenderness. This atraumatic technique is described.

Daily observations were made on fingers not incised. By a special method of estimating the finger-volume patients were divided on admission into those whose fingers were swollen more and less than 10%. The finger swollen less than 10% often never required operation. The finger swollen more than 10% generally required operation in spite of penicillin. Evidence is presented that, even when systemic penicillin is being given, delay in operation after the finger is swollen 20% is harmful to the patient.

We wish to thank Prof. J. R. Squire for much encouragement; Dr. J. P. Bull, of this Unit, and Dr. J. O. Irwin of the London School of Hygiene, for statistical assistance; Sister M. Taylor for her care of the many patients in her ward; and Miss S. Timms for clerical help.

REFERENCES

Bolton, H., Catchpole, B. N., Jepson, R. P. (1947) *Lancet*, ii, 608.
Curr, J. F. (1945) *Edinb. med. J.* **52**, 469.
d'Abreu, F., Flood, C. M., Hewitt, H. B. (1947) *Brit. med. J.* ii, 603.
Florey, M. E., Williams, R. E. O. (1944) *Lancet*, i, 73.
Loudon, J. B., Miniero, J. D., Scott, J. C. (1948) *J. Bone Jt Surg.* **30B**, 409.
Moss, B., Squire, J. R., Topley, E., Johnston, C. M. (1948) *Lancet*, i, 320.
Pilcher, R. S., Dawson, R. L. G., Milstein, B. B., Reddell, A. G. (1948) *Ibid*, p. 777.
Webster, A. L. (1947), *Ibid*, ii, 610.

"... One crucial feature of the difficulty in England, I believe, is that the responsibility for being healthy and economically self-sufficient has been shifted from the patient to his physician. ... There are three groups of cases in which the physician is at a peculiar disadvantage when the patient sheds the responsibility for getting well. In the first of these the person with a purely psychogenic or simulated disorder is thought to have organic disease. ... The converse situation, in which an organic disorder is diagnosed as psychoneurosis by the physician, is also seen with disconcerting frequency. ... But the most difficult group of all is the much larger one of the patients with unequivocal evidence of structural malady in whom the question arises whether the complaints are excessive for the degree of anatomic damage present."—Prof. WILLIAM H. SWEET, *New Engl. J. Med.* 1949, **240**, 168.

Digitized by Google

A CLINICAL METHOD OF ASSESSING ANALGESICS

A. J. H. HEWER
M.B. Lond., D.A.
RESEARCH ANÆSTHETIST, MIDDLESEX HOSPITAL, LONDON

C. A. KEELE
M.D. Lond., F.R.C.P.
LECTURER IN PHARMACOLOGY, MIDDLESEX HOSPITAL MEDICAL SCHOOL, LONDON

K. D. KEELE
M.D. Lond., M.R.C.P.
PHYSICIAN, ASHFORD COUNTY HOSPITAL, MIDDLESEX

P. W. NATHAN
M.B. Lond., M.R.C.P.
MEMBER OF NEUROLOGICAL RESEARCH UNIT, NATIONAL HOSPITAL, QUEEN SQUARE, LONDON

IT is not easy to assess the clinical value of analgesics because pain varies widely in different people for both physiological and psychological reasons, and because patients with comparable pathological painful lesions are difficult to find.

To overcome some of these difficulties various workers have studied the effects of analgesics in trained volunteers in whom pain has been produced by methods in which the intensity of stimulus has been measured as precisely as possible. In the original work on these lines Macht et al. (1916) used a faradic current; Seevers and Pfeiffer (1936) measured the response to graded pressure with von Frey's hairs or a needle prick; and Hardy et al. (1940) applied radiant heat to the blackened forehead. In all these cases the painful stimulus was very brief and was applied to skin, thus producing what Lewis (1942) described as "superficial" pain. Goetzl et al. (1943) applied an alternating current to a dental filling, and Harrison and Bigelow (1943) measured the number of contractions in ischæmic muscle in the forearm required to produce pain; this pain is "deep" in character.

There is little doubt that analgesics raise the threshold to various painful stimuli, but Hardy et al. (1940) have shown that the action of morphine in raising the threshold to "superficial" pain is almost abolished when this drug is given to people enduring experimentally induced pain of another kind—e.g., that which follows contractions of ischæmic muscle. It therefore seems that analgesics act mainly by some mechanism other than that which raises pain thresholds; and indeed Hardy et al. have suggested that relief of pain is due to the detachment of pain perception from a complex anxiety reaction pattern, and to the production of lethargy and sleep. Hewer and Keele (1948) have studied the effects of intravenously injected analgesics on existent ischæmic-muscle pain. They have noted that with small doses of analgesics there is relief of such pain with no detectable side action. This may represent a simple threshold-raising effect. However, with larger doses of analgesics there is also a definite feeling of detachment, and often of euphoria, which may correspond to the type of action suggested by Hardy et al. None of these workers' methods provides direct evidence concerning the action of analgesics on pain experienced by patients.

The investigations here presented are concerned primarily with the development of methods of assessing the effectiveness of analgesics in patients with pain. The main purposes are to demonstrate how pain may be recorded, how results of numerous observations in individual patients or groups of patients may be summarised, how psychological factors may be assessed, and how analgesics may be compared with one another. A new analgesic, 'Physeptone,' * introduced in Germany during the war under the name of 'Amidone,' has been used to illustrate many points, but this paper is not intended to provide exhaustive information on its clinical use.

PAIN CHARTS

In these studies of the actions of analgesics in patients we have relied entirely on their own accounts of the intensity of pain. It was found that intelligent coöperative patients could give consistent reports on the course of their pain which correlated well with the expected effects of known analgesics.

The patients were asked to record the intensity of pain as "none," "slight," "moderate," "severe," or "very severe." For simplification a scale of 0, 1, 2, 3, and 4 units has been used to record these verbal descriptions of the grades of pain, and the results have been presented as pain charts. The value of daily pain charts in summarising the occurrence and severity of pain has been described by Keele (1948), who has also shown how useful such records may be in demonstrating the effects of analgesics.

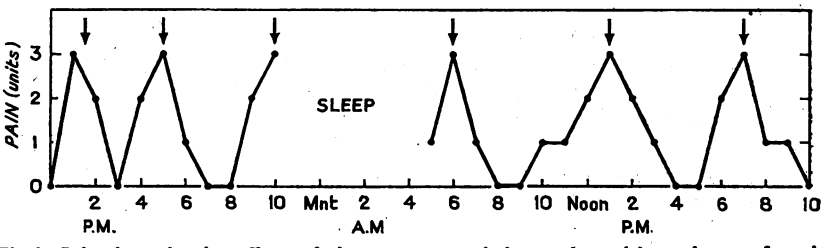


Fig. 1—Pain chart showing effects of physeptone on pain in a patient with carcinoma of cervix uteri: each arrow indicates administration of physeptone 7·5 mg. by mouth.

Records of pain intensity were usually made hourly, but shorter intervals were sometimes useful in determining the times of onset and peak action of drugs. In many cases the patients kept their own charts; in others the coöperation of the nurses was necessary. Fig. 1 shows a typical record of the effect of giving physeptone 7·5 mg. by mouth to a patient with carcinoma of the cervix uteri, invading the right os innominatum and sacral plexus and producing pain in the right lower limb and coccyx. It will be seen that the pain was completely relieved for short periods after the administration of this drug.

Fig. 2 shows the response to physeptone 20 mg. given by mouth to another patient, also with carcinoma of

* Physeptone is *dl*-2-dimethylamino-4 : 4-diphenylheptan-5-one hydrochloride.

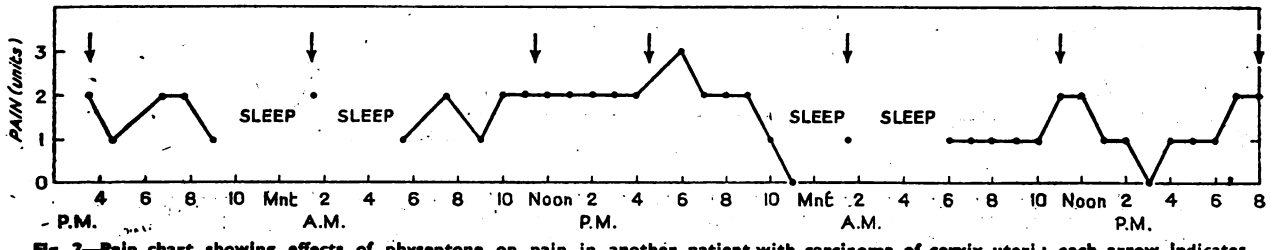


Fig. 2—Pain chart showing effects of physeptone on pain in another patient with carcinoma of cervix uteri: each arrow indicates administration of physeptone 20 mg. by mouth.

Digitized by Google

the cervix uteri. This dose was obviously less effective than 7·5 mg. had been in the first patient, who had a similar type of pain. Indeed, on one occasion the second patient showed an increase in pain intensity 1 hr. 20 min. after receiving physeptone, and the records definitely suggested that there were spontaneous variations in the background of pain.

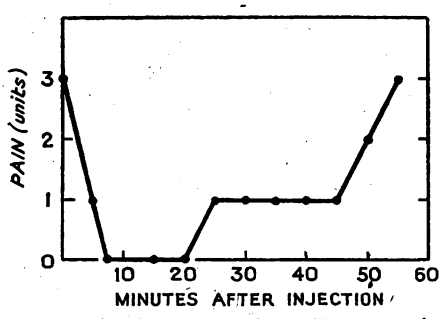


Fig. 3—Pain chart showing effects of intramuscular injection of compound C.B.11 10 mg. in a patient with carcinoma of larynx.

Pain charts are also useful in recording effects at short intervals. In fig. 3 the intensity of pain was recorded at 5-min. intervals from a patient who had pain associated with carcinoma of the larynx. After the intramuscular injection of 10 mg. of 'C.B.11'† the analgesic action developed very rapidly and was complete for a short period, though the pain had returned to its original intensity 55 min. after the injection. An hourly record might clearly miss all such details when a drug of quick onset and brief duration of action is being studied.

CONTROL OBSERVATIONS

In investigations on analgesics in man, control studies are necessary to show the extent of spontaneous variations in pain intensity and to determine the part played by psychological factors in the relief of pain.

Spontaneous Variations

It is usually impossible to make protracted or repeated control observations without offering the patient some alleviation of his pain, but fig. 4 shows a pain chart in a patient with chondrosarcoma of the ilium. No drugs were given during a 3-day period, during which spontaneous variations in pain were clearly seen. Some idea of spontaneous variations may also be obtained by noting the difference in response to repeated administrations of the same dose of an analgesic (fig. 2).

Psychological Factors

The effects of reassurance or of suggestion are difficult to eliminate altogether, since any patient complaining of pain will assume—usually rightly—that the treatment given is designed to relieve pain. One can, however, test the effect of pharmacologically inert materials, such as 0·9% sodium chloride solution or sterile water by injection, or lactose tablets by mouth. The tablets may be made the same size and shape as tablets of a recognised analgesic. In the following observations patients given inert substances were approached in the same way as patients given analgesics.

Fig. 5 illustrates the effects of an intramuscular injection of sterile water in two patients with pain of 3 units intensity. In patient A the pain was felt in the region of an abdominal incision; in patient B it was associated with a large non-malignant gastric ulcer infiltrating the pancreas. In both patients relief of pain was complete and comparable in time course with that commonly seen after the injection of analgesics.

To investigate this factor more fully the effects of 16 mg. of morphine ‡ have been compared with those of sterile water, both being injected intramuscularly in 1 ml. volume, in patients with comparable types of pain. Morphine was given on 33 occasions to 12 patients, and sterile water on 33 occasions to 15 patients; 7 of the patients received both morphine and sterile water. The results are summarised as follows:

Morphine gr. 1/4 Pain (units)			*Sterile water* Pain (units)		
Before injection	*1 hr. after injection*	*No. of occasions*	*Before injection*	*1 hr. after injection*	*No. of occasions*
3	0	19	3	0	14
3	1	3	3	1	5
3	2	4	3	2	4
3	3	2	3	3	7
4	0	1	3	4	1
4	1	1	2	2	1
4	2	1	2	3	1
2	0	2			
Total		33	Total		33

Comparison of the effects of morphine and of sterile water on pain. Pain is expressed in units as described in text. The column "number of occasions" shows the frequencies of the changes in pain intensity following injections.

To allow statistical techniques to be applied to these data it has been postulated that the units of the five-point scale are linearly related to intensity of pain.

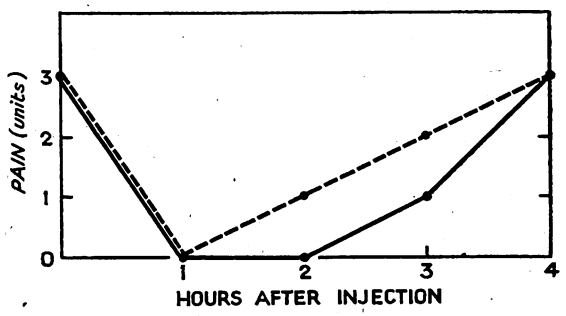


Fig. 5—Pain chart showing effects of injections of sterile water on pain in two patients, A (solid line) and B (interrupted line).

The figures for reduction of pain an hour after injection in each series have been compared statistically, Fisher's (1946) extension of "Student's" t-test for the comparison of the means of two samples being used. The value of P (probability) lies between 0·01 and 0·001. $P = 0.05$ has been taken as the level of significance in all cases; so this result shows that, with enough observations on patients chosen at random, the analgesic action of morphine will be much greater than that produced by the psychological effects of sterile water.

† C.B.11, or 'Heptalgin,' is 6-morpholino-4 : 4-diphenylheptan-3-one hydrochloride (kindly supplied by Glaxo Laboratories Ltd.).

‡ The doses of morphine mentioned here are of the hydrochloride or the sulphate.

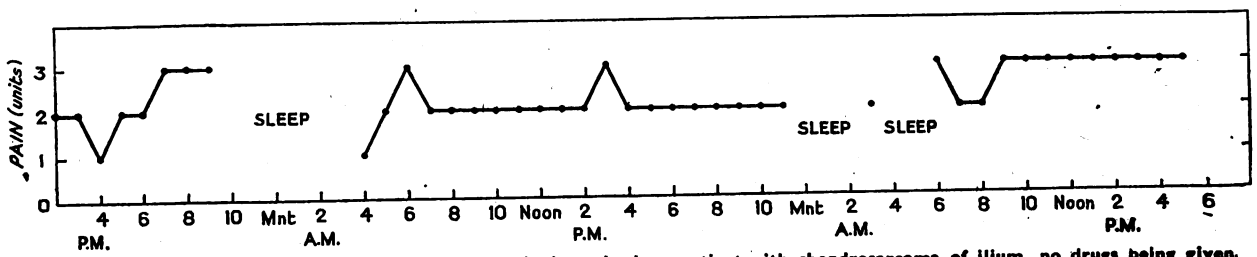


Fig. 4—Pain chart showing spontaneous variations of pain intensity in a patient with chondrosarcoma of ilium, no drugs being given.

Digitized by Google

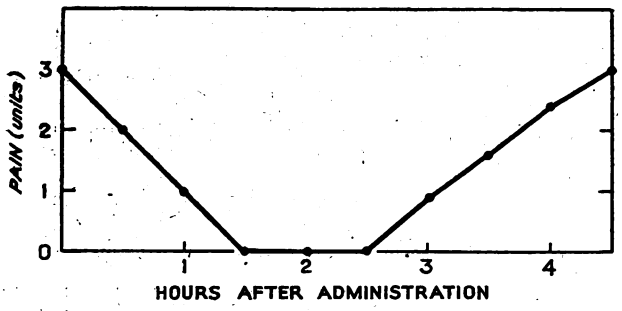


Fig. 6—Composite pain chart showing effects of physeptone: each point represents the mean value of pain units in 18 trials after administration of physeptone 10 mg. by mouth.

In the above results sleep has been recorded as 0 units of pain. If these values are excluded, for reasons discussed later, the value of P lies between 0·02 and 0·01, which still indicates the significantly more powerful effect of morphine.

Some patients show little or no response to inert substances. For example, a patient with rheumatoid arthritis and spondylitis deformans showed no reduction in pain after taking lactose tablets, though physeptone 10 mg. by mouth was invariably followed by complete relief. This observation agrees with those of Hewer and Keele (1948), who noted that injections of sterile water or subthreshold doses of analgesics had no influence on artificially induced ischæmic-muscle pain in normal volunteers.

INTERPRETATION OF SLEEP IN THE RECORDS

Some difficulty arises in the interpretation of "sleep" in the pain charts. The effectiveness of an analgesic can be accepted if it produces sleep in a patient who has been kept awake by pain; but this action is more likely to occur at night than during the day. If it is assumed that during sleep no pain is experienced (0 units on the pain chart), the time of day must be taken into account in assessing the effects of an analgesic. In some patients a drug has reduced pain from 4 to 2 units without producing sleep during the day, and yet at night, when the pain was also 4 units, the same dose of the drug has produced sleep. The point requiring emphasis is that at night, when there is a natural tendency to sleep, the analgesic action of a drug may appear to be greater than by day. In summarising our data we have sometimes excluded readings of "sleep," and at others we have classified "sleep" as "no pain" (0 units).

METHODS OF SUMMARISING RESULTS

Individual pain charts provide a useful graphic demonstration of the degree and duration of analgesic action; but, where numerous records of the effects of a fixed dose of a drug have been obtained, it is clearly necessary to summarise the results in some abbreviated form. This may be done in one of two ways.

(1) The mean values of pain units at half-hourly or hourly intervals after administration of a drug have been taken as the simplest measure of intensity and duration of effect. In cases where pain is continuous, graphic representation of such results illustrates very clearly the course of the drug's action. For example, fig. 6 shows the mean values of pain in 18 trials after physeptone 10 mg. had been given by mouth to the above-mentioned patient with rheumatoid arthritis and spondylitis deformans. Pain was completely relieved at $1^1/_2$, 2, and $2^1/_2$ hours, and then increased progressively to reach the original level of 3 units $4^1/_2$ hours after administration of the drug. The return of pain intensity to the original level on so many occasions suggests a constant intensity of pain against which the analgesic action was exerted. The validity of such records is naturally enhanced by similar responses to other analgesics and by a lack of response to placebos.

Mean values have also been found useful to summarise the effects of a fixed dose of a drug given to different patients. For instance, the results of injecting 20 mg. of physeptone into 15 patients (36 tests) with various types of pain were as follows:

	Before injection	*Hours after injection* 1	2	3	4
Pain units (mean values of 36 tests)	2·9	0·7	0·4	0·6	0·6

Results obtained in this way take no account either of the psychological component in relief of pain or of spontaneous variations in pain intensity, hence they may be more representative of the probable therapeutic effects of the drug.

(2) In individual patients it has been found useful to display the variations in response to a fixed dose of analgesic by presenting the responses to each dose in a frequency table. In this case only the maximal change in pain units within 3 hours of administration of the drug is taken into account.

A frequency table showing the effects of administering 20 mg. of physeptone by injection to a woman with carcinoma of the cervix uteri (same patient as in fig. 2) on 14 occasions gave the following results:

	Maximal changes (pain units)						
	3→0,	3→1,	3→2,	2→0,	2→1,	2→2,	2→3
Frequency	1	3	2	3	3	1	1

The most frequent response was a reduction of pain by 1–2 units.

In another patient the effects of intramuscular injection of 20 and 30 mg. of physeptone were as follows:

	Max. changes (pain units)			
	4→1,	4→2,	4→3,	4→4
Frequency with 20 mg...	4	0	1	1
Frequency with 30 mg...	4	8	0	0

TESTS OF RELIABILITY OF PATIENTS

Where detailed tests of the comparative potency of analgesics were made in individual patients with chronic pain the following criteria of reliability were considered:

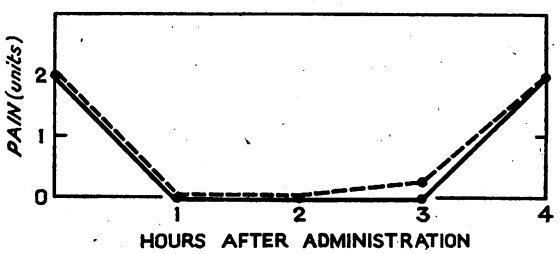


Fig. 7—Composite pain chart showing effects of pethidine in same patient as in fig. 6: solid line, mean values of pain units in 4 trials after administration of pethidine 150 mg. by mouth; interrupted line, mean values of pain units in 8 trials after administration of pethidine 150 mg. by mouth a month after the first series.

(1) Absence of response to inert materials—e.g., sterile water by injection or lactose tablets by mouth—was required. This factor has already been discussed and illustrated.

(2) Constancy of response to the administration of the same dose of the same drug at different times was desirable. The effects of pethidine 150 mg. by mouth in the above-mentioned patient with rheumatoid arthritis and spondylitis deformans are summarised in fig. 7. In one test the mean effects of four separate doses of pethidine were recorded. In a second test, a month later, the mean effects of eight doses were recorded. The values are almost identical for the two series, indicating a satisfactory constancy of response.

Digitized by Google

(3) The ability to distinguish the effects of two different doses of the same drug was necessary. This test is very valuable, and its application is limited mostly by the difficulty of making long observations at the smaller and less effective dose level. A patient with an extensive rodent ulcer involving the right side of the head and orbit had very severe pain which demanded frequent administration of analgesics. On 4 occasions 16 mg. (gr. 1/4) of morphine was injected, and the mean values of pain intensity were as follows:

Before injection of morphine ..	4·0 units
1 hour after " " " ..	3·3 units
2 hours " " " " ..	3·0 units
3 " " " " " ..	3·7 units

He was subsequently given fourteen injections of 32 mg. (gr. 1/2) of morphine, all during waking hours, and the mean values of pain intensity were as follows:

Before injection of morphine ..	4·0 units
1 hour after " " " ..	2·2 units
2 hours " " " " ..	2·2 units
3 " " " " " ..	3·2 units

The difference between the mean values at 1 hour after the administration of 16 mg. and of 32 mg. of morphine has been analysed statistically; with the t-test P was found to lie between 0·02 and 0·01, so the difference can be regarded as significant, 32 mg. being more effective than 16 mg. of morphine.

Another patient showed the following responses to lactose and physeptone given by mouth:

Drug	Hours after administration 0	1	2	3	4	
Lactose ..	2	2	2	2	2	(means of 4 observations)
Physeptone 2·5 mg. ..	2	0·9	0·9	1·9	2	(means of 7 observations)
Physeptone 5 mg. ..	2	0·2	0·1	0·2	2	(means of 19 observations)

Figures are pain units.

The differences between lactose and physeptone need no statistical analysis. The differences between 2·5 and 5 mg. of physeptone were analysed statistically by testing the significance of the difference of the mean values recorded 2 hours after administration. The t-test gave a value for P between 0·02 and 0·01; so the difference was significant, 5 mg. being more effective than 2·5 mg. of physeptone.

COMPARISON OF DIFFERENT ANALGESICS

The comparison of analgesic potency of different analgesics is carried out in a similar way to the comparison of the effects of two doses of the same drug, or the comparison of true analgesics with inert substances. Sometimes the side-effects with one of the drugs prevent an adequate trial. It is impracticable to make repeated observations on patients in whom a particular dose of an analgesic is plainly ineffective. For this reason comparisons are best made by finding a satisfactory dose level for each drug tested, and by making enough observations to give a reasonable estimate of activity.

The method may be applied either by tests in which a number of observations are made on 12–15 patients, each of whom may receive only one of the drugs to be tested, or by testing individual patients to whom two or more drugs may be administered, each for a long period.

The former method may be illustrated by a comparison of the effects of 16 mg. of morphine injected on 33 occasions into 12 patients, with those of physeptone 20 mg. injected on 36 occasions into 14 patients; 8 of these patients received both drugs. Sleep was recorded in this series as 0 units of pain. The results were as follows:

Drug	Hours after injection 0	1	2	3	4	
Morphine gr. 1/4 (16 mg.)	3·0	0·6	0·4	0·4	0·4	(mean values)
Physeptone 20 mg. ..	2·9	0·7	0·4	0·6	0·6	(" ")

Figures are pain units.

The effects of 20 mg. of physeptone were almost identical with those of 16 mg. of morphine, and the small differences apparently favouring the latter were not statistically significant.

To illustrate the other method of comparison of drugs, the results in one patient with severe chronic pain are presented. Physeptone 30 mg., morphine 32 mg., and pethidine 150 mg. were given intramuscularly with the following results:

Drug	Hours after injection 0	1	2	3	4
Morphine 32 mg.	4·0 (14)	2·2 (14)	2·2 (14)	3·2 (12)	3·3 (4)
Physeptone 30 mg. ..	4·0 (17)	2·2 (17)	2·3 (16)	2·4 (14)	3·3 (10)
Pethidine 150 mg. ..	3·9 (7)	2·7 (7)	2·4 (7)	2·7 (7)	3·3 (4)

The figures are mean values, in pain units, for each period after the injection. The figures in parentheses are the number of observations.

It will be noted that here the relief of pain was only moderate; this patient preferred such a moderate response to a greater analgesic effect coupled with the side actions which resulted when large and analgesically more effective doses were given.

The results may also be analysed by means of a frequency table in which the maximal changes within three hours of injection are recorded:

Drug	Maximal changes (pain units) 4→0	4→1	4→2	4→3	4→4	3→4
Morphine 32 mg. ..	0	4	9	1	0	0
Physeptone 30 mg. ..	0	4	13	0	0	0
Pethidine 150 mg. ..	0	1	3	2	0	1

Figures are frequencies.

The effects of physeptone 30 mg. and pethidine 150 mg. were compared statistically from these data by the method described for comparing two doses of morphine. The value of P for the comparison of the two means lies between 0·02 and 0·01, which can be regarded as significant, 30 mg. of physeptone being more effective than 150 mg. of pethidine.

It seems justifiable to draw the following conclusions about the actions of these drugs in this patient: (1) that 30 mg. of physeptone was about as effective as 32 mg. of morphine; (2) that 30 mg. of physeptone, and therefore 32 mg. of morphine too, were significantly more effective than 150 mg. of pethidine.

The patient's general impression, which also took account of side-effects, placed the effectiveness of the drugs in the following order: (1) 30 mg. of physeptone; (2) 32 mg. of morphine (not far behind physeptone); and (3) 150 mg. of pethidine (some way behind the other two drugs).

A good illustration of a clear difference between the effectiveness of two drugs is provided by a comparison of the actions of pethidine hydrochloride 100 mg. and codeine phosphate 97·5 mg. (gr. 1 1/2), which were both given by mouth to another patient. The results were as follows:

Drug	Hours after administration 0	1	2	3	4	
Pethidine 100 mg. ..	3	0	0	0	2	(means of 4 experiments)
Codeine gr. 1 1/2 ..	3	2	2	2	3	(means of 3 experiments)

Figures are pain units.

In this patient 100 mg. of pethidine hydrochloride was much more effective than 97·5 mg. of codeine phosphate.

DISCUSSION

These studies show how more precise information than is usually recorded can be obtained concerning the influence of analgesics on the course of pain. The speed of onset, the time of peak effect, and the total duration of action of a given drug are easily seen in individual pain charts. In selected patients with chronic pain the

Digitized by Google

mean values of numerous records provide data helpful for comparing the effectiveness of different drugs. The variations in individual responses to analgesics and the sometimes striking effects of inert materials might vitiate the results; but, if the records are obtained from a large enough group of patients such discrepancies would be smoothed out. It may therefore be possible to compare the effectiveness of analgesics, either by obtaining numerous records on a few selected patients with chronic pain or by obtaining relatively few observations on numerous patients.

A somewhat comparable method for clinical testing of analgesic drugs in large numbers of patients has been described by Lee (1942), who compared the effectiveness of morphine, methyldihydromorphinone ('Metopon'), and dihydrodesoxymorphine (desomorphine). He recorded the degree of relief of pain in terms of "none," "slight," "fair," or "complete," and noted the duration of action of the drugs, the occurrence of sleep and of side-effects, and the development of tolerance and physical dependence (as shown by the abstinence syndrome on withdrawal of the drug).

In both methods the results obtained with each drug are added together, and these figures are susceptible to statistical analysis. This analysis has, in all instances tested, given results in agreement with the general clinical impressions of the relative values of analgesics. The permanent records obtained by the methods described largely eliminate the factor of memory on which general impressions depend. It is important to exclude the memory factor when one drug is compared with another at intervals exceeding a few days. As Lewis (1942) has emphasised:

> "One reason for inaccuracy and inadequacy of description [of pain] is the difficulty of calling up exact memories of what has been felt some time previously. It is certain that the closer the description is to the event the more accurate it becomes and that the description is most accurate when given at the time pain occurs. . . ."

SUMMARY

Subjective pain-intensity scales have been developed and used to provide data to construct pain charts, which are of value in assessing the effects of analgesics.

Illustrations are given to show how such factors as spontaneous variations in pain intensity and psychogenic influences may be allowed for, and methods are described for summarising the data so that the effects of different analgesics may be compared statistically, either in selected patients, to each of whom several drugs are given, or in groups of patients who may individually receive only a few doses of the drug under investigation.

Many of the points discussed have been illustrated by observations on the comparative effects of morphine, pethidine, and physeptone.

We wish to thank Prof. P. B. Ascroft and Prof. B. W. Windeyer, of Middlesex Hospital, and medical officers of Middlesex County Hospitals for access to their patients; the nurses of these hospitals for their help in keeping records; Mr. W. F. Floyd, B.SC., of the department of physiology, Middlesex Hospital Medical School, for help in the statistical aspects of this paper; and Dr. E. A. Carmichael, of the National Hospital, Queen Square, for helpful criticisms.

REFERENCES

Fisher, R. A. (1946) Statistical Methods for Research Workers. 10th ed., Edinburgh and London; sec. 24, p. 1.
Goetzl, F. R., Burrill, D. Y., Ivy, A. C. (1943) *Quart. Bull. Nthwest. Univ. med. School*, **17**, 280.
Hardy, J. D., Wolff, H. G., Goodell, H. (1940) *J. clin. Invest.* **19**, 649.
Harrison, I. B., Bigelow, N. H. (1943) *Proc. Ass. Res. nerv. ment. Dis.* **23**, 154.
Hewer, A. J. H., Keele, C. A. (1948) *Lancet*, ii, 683.
Keele, K. D. (1948) *Ibid*, p. 6.
Lee, L. E. (1942) *J. Pharmacol.* **75**, 161.
Lewis, T. (1942) Pain. London.
Macht, D. I., Herman, N. B., Levy, C. S. (1916) *J. Pharmacol.* **8**, 1.
Seevers, M. H., Pfeiffer, C. C. (1936) *Ibid*, **56**, 166.

MARCH HÆMOGLOBINURIA

M. LUBRAN
M.B., B.Sc. Lond.
LATE MAJOR R.A.M.C., PATHOLOGIST

J. SAKULA
M.D. Lond., M.R.C.P., D.C.H.
LATE MAJOR R.A.M.C., MEDICAL SPECIALIST

From a Military Hospital in the United Kingdom

HÆMOGLOBINURIA after exercise in an apparently normal man was first described by Fleischer (1881). Occasional cases have since been reported, and in 1941 Gilligan and Blumgart collected 40 published cases and added 3 of their own. It was expected that the intensive training of large numbers of young men during the war would bring to light many more examples, but only 9 further cases have been reported (Palmer and Mitchell 1943, Makin 1944, Bryce 1944, Hobbs 1944, Lindahl and Fatter 1945, Fleming and Kinsman 1945). The admission, therefore, of 3 cases within about a fortnight to one military hospital seemed remarkable and the opportunity was taken of making quantitative observations.

Hitherto the condition has been described only in healthy young men without any evidence of organic disease. Attacks of hæmoglobinuria are brought on by exercise, usually vigorous, in the upright position. Running, marching, and walking may produce an attack, whereas cycling and swimming, even though strenuous, will not do so. The hæmoglobinuria is associated with a rise in the plasma-hæmoglobin level which occurs during the exercise. The condition is benign, and, after running a course ranging from several months to a few years, it appears to clear spontaneously.

THE THREE PATIENTS

Case 1.—A private soldier, aged 18, who had been in the Army six months and was still in training, was admitted to hospital on April 25, 1947, with five weeks' history of passing "blood in his urine" after route marches, the discoloration lasting three or four hours. Apart from this he felt perfectly well and had no other urinary symptoms. There was no past history of any serious illness, and though he had been a keen athlete he had never noted this condition before.

He looked fit and was of average build and normal posture; height 72 in., weight 152 lb. No abnormal signs were detected. There was no jaundice, the spleen was not palpable, and the blood-pressure was 125/75 mm. Hg. A plain radiogram of his renal tract was normal.

Case 2.—A private soldier, aged 18, who had been in the Army for six months was admitted, also on April 25, 1947, with six weeks' history of passing "blood in his urine" after route marches and football. The discoloration of his urine had lasted two or three hours and had been accompanied by a dragging pain in the right groin. Apart from slight urinary frequency he had no other symptoms. His past medical history was negative, and he too had been a keen athlete.

He looked fit and was of average build and normal posture; height 70 in., weight 158 lb. No abnormal signs were detected. There was no jaundice or splenomegaly, and his blood-pressure was 120/70 mm. Hg. A plain radiogram of his renal tract was normal.

Case 3.—An aircraftman, aged 20, who had been in the R.A.F. for a year and a half was admitted on May 10, 1947, with a week's history of his urine being red after he had been travelling. The travelling had followed severe exercise. Apart from this he had no other symptoms, and his past history was negative except for a slight attack of "hæmaturia" in November, 1946.

He was of average build and normal posture but looked rather pale. Height 66 in., weight 134 lb. His blood-pressure was 120/80 mm. Hg. There were a soft systolic murmur over the apex of the heart and a venous thrill in the vessels of the neck. Nothing else abnormal was found except that the tip of his spleen was palpable.

Digitized by Google

INVESTIGATIONS

In addition to the clinical examinations, each case underwent a full hæmatological and urinary investigation soon after admission. The findings were as follows:

Investigation	*Case 1*	*Case 2*	*Case 3*
Red cells per c.mm.	4,500,000	4,640,000	3,200,000
Hæmoglobin (g. per 100 ml.)	13·5	14·0	8·4
M.C.H. (μμ g.)	30	30	26
Packed cell vol. (ml. per 100 ml.)	40	39	28
M.C.V. (c. μ)	89	84	87
Mean cell diameter (μ)	7·2	7·0	7·0
Reticulocytes (% of red cells)	0·1	0·1	3·2
Red-cell fragility:			
Hæmolysis starts (% NaCl)	0·40	0·40	0·42
Hæmolysis ends (% NaCl)	0·34	0·34	0·32
Platelets (per c.mm.)	220,000	200,000	240,000
White cells (per c.mm.)	6800	7200	4600
Plasma-bilirubin (mg. per 100 ml.)	0·2	0·2	0·6
Wassermann reaction	Neg.	Neg.	Neg.
Kahn test	,,	,,	,,
Rosenbach test *	,,	,,	,,
Donath-Landsteiner reaction †	,,	,,	,,
Plasma-ascorbic acid (mg./100 ml.) ‡	0·2	0	0
Urine:			
Sp. gr.	1·020	1·024	1·018
protein	Nil	Nil	Nil
colour	Amber	Amber	Amber
benzidine test	Neg.	Neg.	Neg.
ascorbic acid §	Nil	Nil	Nil
deposit	No casts, red cells, white cells, or pus.		

* Test carried out by immersing arm or leg in ice-cold water for 30 min. and then examining urine, passed immediately after, for hæmoglobin.

† Carried out by Sanford's method (Whitby and Britton 1942).

‡ Determined by Roe's dinitrophenyl-hydrazine method (Dyke 1947).

§ Determined by usual indophenol-dye method.

The findings were normal except for the plasma-ascorbic-acid values, which were low, and the fact that case 3 had a well-marked anæmia, which improved under treatment with ferrous sulphate gr. 6 t.d.s., the amount of hæmoglobin being 13·2 g. per 100 ml. and the red-cell count 4,200,000 per c.mm. on his discharge from hospital.

The amount of hæmoglobin in the plasma and in the urine was measured before and after exercise by the method of Bing and Baker (1931) and Bing (1932) in case 3, while in cases 1 and 2 approximate values were obtained by diluting the patient's blood until it matched the plasma in colour. An analogous method was used for the urine in cases 1 and 2. Blood was taken from a vein with an oiled syringe to prevent artificial hæmolysis and transferred to a heparinised container. Repeated checks on the method in normal persons showed plasma-hæmoglobin levels consistently below 10 mg. per 100 ml., the accepted upper limit of normality.

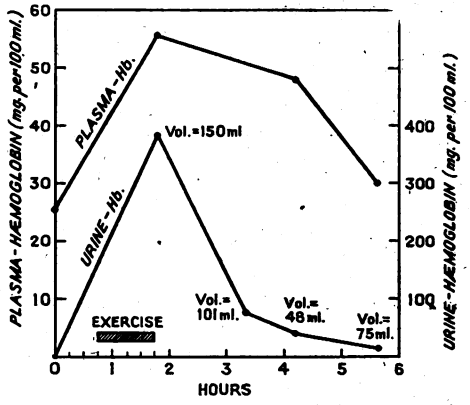
No spontaneous attacks of hæmoglobinuria developed during the patients' stay in hospital, but attacks could be induced, as required, by getting them to perform a standard exercise consisting of running and walking about 6 miles in an hour.

Blood and Urine Findings During Attack

Experiments showed that during an attack hæmoglobinuria was associated with a rise in the plasma-hæmoglobin level, as follows:

	Case 1	*Case 2*	*Case 3*
Before exercise:			
Plasma-Hb (mg per 100 ml.)	<10	<10	9·0
Urine: colour	Amber	Amber	Amber
Hb	Nil	Nil	Nil
sp. gr.	1·024	1·016	1·020
protein	Nil	Nil	Nil
deposit	No red cells, casts, or white cells		
After exercise:			
Plasma-Hb (mg. per 100 ml.)	About 30	About 50	227
Urine: colour	Pale red	Light red	Dark red
Hb (mg. per 100 ml.)	About 100	About 300	1100
protein	+	+	+ + +
deposit	No red cells, casts, or white cells		

The rates of production of hæmoglobinæmia and hæmoglobinuria were determined on one occasion in case 3, after the standard exercise (see figure). The high initial value for plasma-hæmoglobin (25 mg. per 100 ml.) was probably due to the patient's running 200 yards to the laboratory to be on time for the test, since his usual resting level was about 9 mg. per 100 ml. The graph shows that hæmoglobinuria was present as long as the plasma-hæmoglobin level was higher than about 30 mg. per 100 ml., which can be taken as a rough value for the renal threshold in this patient. The



Production of hæmoglobinæmia and hæmoglobinuria in case 3 after an hour's exercise.

total quantity of hæmoglobin passed in the urine during this experiment was equivalent to the hæmolysis of about 6 ml. of blood. The blood-hæmoglobin that day being 12 g. per 100 ml., the rise in plasma-hæmoglobin level would be brought about by the hæmolysis of about 13 ml. of blood, when allowance is made for the hæmoglobin excreted in the first hour's urine and if the plasma volume is assumed to be 3 litres.

Effect of Posture

All observers agree that the upright posture is essential for the development of this type of hæmoglobinuria. This was so in our three cases. The patients were made to exercise vigorously, in a kyphotic position, on a stationary bicycle until they were exhausted, but no subsequent hæmoglobinuria or proteinuria was observed. In case 3 the final plasma-hæmoglobin level was 8·6 mg. per 100 ml., showing that this kind of exercise did not produce more hæmoglobinæmia than is normal. Subsequently the standard exercise produced hæmoglobinuria in all three cases.

Effect of Administration of Ascorbic Acid

On the morning of May 15, 1947, an ascorbic-acid saturation test was done on cases 1 and 2. Each was given 700 mg. of ascorbic acid by mouth, and the ascorbic acid passed in the urine during the next four hours was estimated. Case 1 excreted only 8·2 mg., and case 2 only 9·9 mg. of ascorbic acid, indicating a deficiency of the vitamin in each. Both patients performed the usual standard exercise in the afternoon, and, for the first time, no hæmoglobinuria was produced. The standard exercise was repeated next day with the same result. On May 17, both patients were given 250 mg. of ascorbic acid by mouth, and this dose was continued until they were discharged from hospital. Exercise tests were carried out at short intervals after the administration of ascorbic acid, and subsequent examinations of the urine showed that the hæmoglobinuria disappeared completely in case 1 and was considerably diminished in case 2, finally disappearing after about three weeks. After June 11 it was found impossible to produce hæmoglobinuria in either patient, even after much severer exercise than had been taken before. On this day the plasma-hæmoglobin levels were determined before and after exercise, as follows:

	Case 1		*Case 2*	
	Plasma	*Urine*	*Plasma*	*Urine*
Hb (mg. per 100 ml.):				
Before exercise	5·7	Nil	3·2	Nil
After exercise	4·5	Nil	6·2	Nil

No protein was found in any of these specimens of urine.

Digitized by Google

These results show that, with the patients saturated with ascorbic acid, exercise did not cause a significant rise in the plasma-hæmoglobin level. The figures obtained are, in fact, those of normal persons.

On June 15, case 3 was given 250 mg. of ascorbic acid by mouth, and this dose was continued daily until his discharge from hospital. The curve shown in the figure had been obtained on June 11, and hæmoglobinuria had been produced by exercise on the 14th. On June 16, after 500 mg. of ascorbic acid had been taken, the standard exercise did not produce either hæmoglobinuria or proteinuria. The same result was obtained after exercise on June 19:

Date	*Time*	*Plasma-Hb (mg. per 100 ml.)*
June 16 ..	Before exercise	3·0
	After 1 hour's exercise ..	15·6
	1 hour later	4·0
June 19 ..	Before exercise	3·0
	After 1 hour's exercise ..	2·8

No Hb or protein was found in any specimen of urine passed during these tests.

As with cases 1 and 2, it was found impossible, after saturation with ascorbic acid, to produce hæmoglobinuria even by severe exercise.

DISCUSSION

Diagnosis

The characteristic history and the absence of signs and symptoms of other varieties of paroxysmal hæmoglobinuria establish these three cases, without doubt, as cases of march hæmoglobinuria. Case 3 was unusual in having a considerable anæmia, a feature which has not previously been reported. The quantity of blood lost on each occasion of hæmoglobinuria seldom exceeds 30 ml. However, repeated losses of this order at short intervals were probably responsible for the anæmia in this case.

The differential diagnosis of march hæmoglobinuria has been adequately discussed by Gilligan and Blumgart (1941). The Rosenbach test and Donath-Landsteiner reaction readily enable the condition to be distinguished from paroxysmal hæmoglobinuria due to cold (syphilitic type), and the other kinds of paroxysmal hæmoglobinuria do not occur in apparently healthy people.

Etiology

The cause of march hæmoglobinuria is unknown. Though the upright posture is essential for its production the condition is not related to orthostatic albuminuria. Most of the reported cases and the three recorded here did not show orthostatic albuminuria, and cystoscopy has shown that in an attack of march hæmoglobinuria hæmoglobin is passed in the urine from both kidneys, whereas in orthostatic albuminuria only urine coming from the left kidney contains protein. Further, lordosis is usually present in orthostatic albuminuria but is uncommon among persons with march hæmoglobinuria, and it was not present in the three cases described here.

There is no doubt that, in march hæmoglobinuria exercise in the upright position is associated with hæmolysis, and that the resulting rise in the plasma-hæmoglobin level leads to the hæmoglobinuria. Witts (1936) suggested that, because of the triviality of the symptoms, there could not be much free hæmoglobin in the plasma, but he thought there was a local hæmolysis in the renal vessels, with the prompt excretion of most of the hæmoglobin in the urine and only a small leak into the general circulation. However, quantitative measurements show that hæmoglobinuria is always preceded by hæmoglobinæmia above the normal, and that there is a definite renal threshold for hæmoglobin of about 30 mg. per 100 ml. The threshold for normal people, on the other hand, is about 100 mg. per 100 ml. according to Gilligan and Blumgart (1941), who by injecting hæmoglobin into the circulation also showed that levels of hæmoglobinæmia equal to those met with in march hæmoglobinuria could be produced in normal people without ill effects.

Palmer and Mitchell (1943) suggest that march hæmoglobinuria may be due to a failure of the tissues to remove the hæmoglobin normally liberated from effete red cells into the blood-stream. They postulate that, as a result of exercise in the upright position, the "removal system" becomes blocked and hæmoglobin accumulates in the plasma. By assuming the life of a red cell to be about 30 days and the plasma volume to be 3 litres they calculated that an hour's exercise could produce a plasma-hæmoglobin level of about 30 mg. per 100 ml. Their suggestion, however, is improbable, since it could not explain the plasma-hæmoglobin level of 227 mg. per 100 ml. found in case 3, or the equally high levels found by other observers. If, as is probable, the average life of a red cell is over 100 days (Shemin and Rittenberg 1946), their hypothesis has no foundation.

March hæmoglobinuria can hardly be due to a circulating hæmolysin, for no investigator has succeeded in demonstrating one; nor can it be due to disordered muscle metabolism, since the urinary pigment has been definitely identified as oxyhæmoglobin and not myoglobin (Gilligan and Blumgart 1941, Witts 1936).

Gilligan et al. (1943) showed that of 22 marathon runners after a 26-mile run, 18 had a plasma-hæmoglobin level above 10 mg. per 100 ml., the average for the group being 14 mg. per 100 ml. and the highest 44 mg. per 100 ml.; 3 were found to have slight hæmoglobinuria corresponding to the hæmolysis of only a few ml. of blood. All blood investigations in these men, including red-cell fragility, gave normal results. These investigators suggest that, in predisposed people this apparently normal response to severe exercise is exaggerated, and march hæmoglobinuria results. They did not explain how hæmolysis is produced.

We wish to present a new, though incomplete, hypothesis of the mechanism involved in march hæmoglobinuria. Though measurements of red-cell fragility are always normal in this condition, such measurements would not detect the presence in blood of a small percentage (of the order of 1%) of highly fragile cells. Therefore the presence of a few such cells cannot be ruled out in march hæmoglobinuria. Mellgren (1939) showed that highly fragile red cells were produced by the spleen, since blood expelled from the spleen underwent spontaneous hæmolysis on standing in vitro. Though there is no convincing evidence that splenic contraction and therefore the discharge of splenic blood into the circulation, takes place under normal conditions in man, the spleen can contract as is seen at operation in cases of congenital hæmolytic jaundice, where manual manipulation of the spleen causes it to contract (Sharpe et al. 1939).

Our hypothesis is that, in persons subject to march hæmoglobinuria, exercise in the upright position causes the spleen to contract and discharge into the circulation a few highly fragile red cells. The hæmolysis of these in the general circulation raises the plasma-hæmoglobin level. The discharge of the splenic blood lasts only for the duration of the exercise, and to account for the observed figures not more than 40 ml. need enter the circulation. The stimulation of the spleen is mechanical rather than nervous and in susceptible persons the amount of manipulation of the spleen associated with moderate exercise in the upright position is enough to cause it to contract. Very severe exercise in normal people might also be sufficient, which would explain the findings of Gilligan et al. (1943) in marathon runners.

In most of the published cases of march hæmoglobinuria the condition seemed to regress spontaneously after a variable period. There are several possible explanations of this. There may be a gradual change in anatomical relationship of the spleen, leading to less mechanical

Digitized by Google

stimulation with exercise, or the spleen may become adapted to the stimulation and so respond less readily. It may also be that the sensitivity of the spleen to contract may be related to the amount of ascorbic acid in the body. Probably a special combination of factors must be present simultaneously for march hæmoglobinuria to occur.

Effect of Ascorbic Acid

The three cases reported here all showed a rapid and dramatic cessation of hæmoglobinuria after large doses of ascorbic acid had been given. Plasma and urine ascorbic-acid determinations, and the ascorbic-acid saturation tests in cases 1 and 2, showed that there was an initial deficiency of ascorbic acid. Measurements of plasma-hæmoglobin after exercise, when the patients had been saturated with ascorbic acid, showed that the rise in the plasma-hæmoglobin level was within normal limits. The effect of ascorbic acid therefore seems to be to lessen the amount of hæmolysis or to diminish the sensitivity of the spleen. The low renal threshold to hæmoglobin in march hæmoglobinuria may be related to a deficiency of ascorbic acid.

Ascorbic acid has been tried previously in two other cases. Hoffmann (1937) said his patient showed considerable improvement after 6 days' treatment with vitamin C intravenously and by mouth, but he did not state the dose. On the other hand, Palmer and Mitchell (1943) gave a patient vitamin C 600 mg. by mouth daily for 16 days and did not observe any change in the hæmoglobinuria.

It is possible that in our patients the administration of ascorbic acid coincided with a spontaneous remission, but this seems unlikely since they all had their usual hæmoglobinuria shortly before the ascorbic acid was given, and all stopped having hæmoglobinuria after they had been saturated with ascorbic acid. Further study on other cases, however, is required before the value of ascorbic-acid therapy can be determined.

SUMMARY

Three new cases of march hæmoglobinuria are described.

One of the patients had a considerable anæmia; the other two conformed to the general description of the condition.

Hæmoglobinuria stopped immediately after the administration of ascorbic acid in two cases. In the third case it stopped in about 3 weeks.

To explain march hæmoglobinuria, it is suggested that in susceptible persons exercise causes the spleen to contract and expel a small number of highly fragile red cells into the blood-stream.

The therapeutic effect of ascorbic acid requires further study.

Our thanks are due to Lieut.-Colonel A. J. A. Gray, R.A.M.C., for permission to publish these cases.

REFERENCES

Bing, F. C. (1932) *J. biol. Chem.* **95**, 387.
— Baker, R. W. (1931) *Ibid*, **92**, 589.
Bryce, L. M. (1944) *Med. J. Aust.* ii, 49.
Dyke, S. C. (1947) Recent Advances in Clinical Pathology. London p. 187.
Fleischer, R. (1881) *Berl. klin. Wschr.* **18**, 691.
Fleming, R. G., Kinsman, J. M. (1945) *Sth. med. J.* **38**, 739.
Gilligan, D. R., Altschule, M. D., Katersky, E. M. (1943) *J. clin. Invest.* **22**, 859.
— Blumgart, H. L. (1941) *Medicine, Baltimore*, **20**, 341.
Hobbs, R. E. (1944) *Amer. J. clin. Path.* **14**, 485.
Hoffmann, W. (1937) *Med. Welt*, **11**, 1640.
Lindahl, W. W., Fatter, M. E. (1945) *J. Urol.* **53**, 805.
Makin, M. (1944) *Brit. med. J.* i, 844.
Mellgren, J. (1939) *J. Physiol.* **94**, 483.
Palmer, R. A., Mitchell, H. S. (1943) *Canad. med. Ass. J.* **49**, 465.
Sharpe, J. C., McLaughlin, C. W. jun., Cunningham, R. (1939) *Arch. intern. Med.* **64**, 268.
Shemin, D., Rittenberg, D. (1946) *J. biol. Chem.* **166**, 627.
Whitby, L. E. H., Britton, C. J. C. (1942) Diseases of the Blood. 4th ed., London; p. 258.
Witts, L. J. (1936) *Lancet*, ii, 115.

INHALATION OF STOMACH CONTENTS

A. WILLCOX
M.A., M.D. Camb., F.R.C.P.
ASSISTANT PHYSICIAN, MIDDLESEX HOSPITAL, LONDON

INHALATION of stomach contents is an unusual accident in these days, though it is said to be commoner in obstetric than in general surgical practice (Mendelson 1946). It can cause alarming symptoms and signs, as in the two cases described here.

CASE-RECORDS

Case 1.—A primigravida, aged 26, was admitted to the maternity ward of the Middlesex Hospital on Nov. 15, 1946, labour having started at 5.15 A.M. She was a healthy woman with no physical abnormality, blood-pressure 130/70 mm. Hg, urine normal. The pregnancy had been normal. Because of delay in the second stage a low forceps delivery was made at 12.25 P.M. under nitrous oxide, oxygen, and ether anæsthesia.

While still partially anæsthetised the patient vomited fluid, some of which she inhaled. She became blue but with postural drainage she expelled a few ounces, her colour recovered, and she returned to the ward in good condition. Two hours later, at 2.50 P.M., she suddenly became distressed, dyspnœic, and deeply cyanosed, with respirations 60, pulse-rate 140, temperature 100°F, and blood-pressure 135/80. There were moist sounds and rhonchi throughout the chest. She coughed persistently but ineffectually, producing only a little sticky sputum. Postural drainage was equally ineffective and had to be abandoned because of the distress it caused.

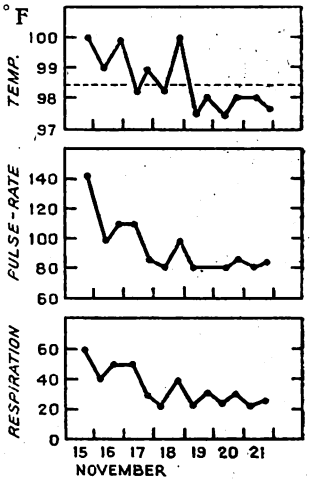


Fig. 2—Temperature chart (case 1).

Two hours later the percussion note was impaired at both bases, especially on the right side. Radiography of the chest showed patchy consolidation throughout both lung fields, particularly at the bases and on the right side (fig. 1). She was given oxygen by nasal catheter and atropine subcutaneously with some relief, and intramuscular penicillin was given as a prophylactic. She remained acutely ill for the next twenty-four hours. Then the cyanosis lessened, the pulse-rate and respirations decreased and the fever fell by lysis (fig. 2). The chest was clinically clear in six days. The patient left hospital on Nov. 29, when radiography showed the lungs to be normal.

Case 2.—A primigravida, aged 26, was admitted to the maternity ward of the Middlesex Hospital on Sept. 9, 1947,

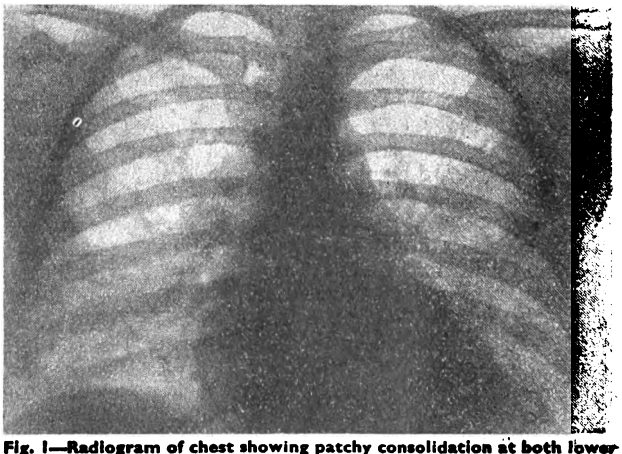


Fig. 1—Radiogram of chest showing patchy consolidation at both lower zones (case 1).

Digitized by Google

She had attended the antenatal department throughout her pregnancy, which had been normal until this day, when albuminuria and a blood-pressure of 165/110 (previously 120/75) were found. Since labour was a week overdue the membranes were ruptured, and late at night on Sept. 10 a lower-segment cæsarean section was performed under thiopentone, oxygen, nitrous oxide, and ether anæsthesia.

While recovering from the anæsthetic the patient vomited and inhaled some fluid. Three hours later she became suddenly dyspnœic and cyanosed, with respirations 30, pulse-rate 130, and temperature 100·8°F. The percussion note was impaired and the air entry weak at the right base, and moist sounds and rhonchi were heard throughout the chest. The blood-pressure was 150/80 and the blood-urea 33 mg. per 100 ml. Sputum was tenacious and scanty. Oxygen intranasally gave some relief, and intramuscular penicillin was given, but the patient remained febrile, cyanosed, and dyspnœic for four days.

Radiography of the chest on the first day showed a patchy consolidation in both lungs, particularly at the bases. By Sept. 22 the lungs were clinically and radiologically clear, and the patient left hospital on Oct. 4, when her blood-pressure was 130/80 and her urine normal.

DISCUSSION

In both patients inhalation of fluid from the stomach was followed, after two or three hours, by an acute pulmonary œdema and bronchial spasm. Fever lasted for four days, and signs persisted in the lungs for six to twelve days. During the first twenty-four hours the patients were desperately ill. Eason and Karp (1943) describe such a case, in which they thought that the pulmonary œdema was due to left ventricular failure. Mendelson (1946), however, has collected 66 cases in which stomach contents were aspirated during labour and in which an acute asthma-like reaction was the usual result: 6 patients developed pneumonia, and 2 had lung abscess, but only 2 died. Suspecting that the acid of the gastric juice was responsible Mendelson instilled gastric contents into the trachea of rabbits, producing a similar reaction, which also followed the instillation of $N/10$ hydrochloric acid. At necropsy the lungs showed bronchiolar spasm and peribronchial congestion, with exudation and hæmorrhage into the lungs. The changes resembled those of chlorine and phosgene poisoning but with rather less epithelial necrosis. Instillation of neutral fluid caused only a temporary dyspnœa.

It therefore seems that the acid in the gastric juice acts as a lung irritant like phosgene, causing pulmonary œdema (Cameron 1948). The clinical picture in the present 2 cases was indeed reminiscent of accounts of phosgene poisoning (Medical Manual of Chemical Warfare 1940), particularly in the delay in the onset of symptoms and in the intense cyanosis. The differentiation from acute left ventricular failure, which was at first suspected in case 2, was difficult, but the absence of any obvious cause of heart-failure, the history of inhaled vomitus, and the radiogram, which showed patchy basal congestion instead of the perihilar œdema of left ventricular failure, suggested the likely cause.

As regards treatment, Mendelson (1946) points out that there is delay in the emptying of the stomach during labour. The custom of feeding patients in labour is therefore risky and should be abandoned. If vomit is inhaled, immediate bronchoscopic aspiration is valuable. If this is impracticable, postural drainage should be done. Once pulmonary œdema has developed, bronchoscopy is unlikely to help and may even be dangerous. Oxygen, antispasmodics, and prophylactic chemotherapy are indicated at this stage.

I am indebted to Mr. F. W. Roques for permission to record these cases and to Dr. H. K. Graham Hodgson for the radiogram.

REFERENCES

Cameron, G. R. (1948) *Brit. med. J.* 1, 965.
Eason, E., Karp, M. (1943) *Anesthesiology*, 4, 508.
Medical Manual of Chemical Warfare (1940) London.
Mendelson, C. L. (1946) *Amer. J. Obstet. Gynec.* 52, 191.

A TUBERCULIN-NEUTRALISING FACTOR IN THE SERUM OF PATIENTS WITH SARCOIDOSIS *

A. Q. WELLS M.A., D.M. Oxfd
J. A. H. WYLIE M.D. Lond.

From the Sir William Dunn School of Pathology, Oxford University

IN the course of investigations into the ætiology of sarcoidosis, we found that the serum of patients with sarcoidosis could modify or even neutralise the ability of Old Tuberculin (O.T.) to evoke a typical reaction in the skin of persons known to be hypersensitive.

First, we observed that a saline extract of a spleen, removed at operation from a patient with sarcoidosis because of an unusual degree of splenomegaly, when mixed in vitro with the appropriate amount of O.T. evoked a greatly diminished reaction in the skin of a sensitised guineapig. The reaction was compared with that produced by the same amount of O.T. diluted with saline and injected into an adjacent area of skin simultaneously. We found also that the neutralising effect was greatest after the splenic extract and the O.T. had been allowed to remain in contact for 48 hours before intracutaneous injection. Extracts made from normal and tuberculous splenic tissue did not neutralise O.T.

We therefore decided to repeat the experiments, with serum from patients with sarcoidosis. Owing, however, to the divergence of opinion as to what justifies a diagnosis of sarcoid, we adopted the following criteria:

(1) Typical clinical appearance and radiological confirmation.
(2) Absence of tubercle bacilli on microscopy, culture, and inoculation of guineapigs.
(3) Mantoux negative to 1 in 100 O.T.
(4) When possible, histological confirmation from biopsy material.

Human skin is more satisfactory than guineapig skin for this test. The skin sensitivity of hypersensitive persons not suffering from tuberculosis is more stable and of a higher degree than that of the infected guineapig. This enables smaller quantities of O.T. to be used, and the same person can be used repeatedly for tests. People sensitive to 1 in 10,000 O.T. were found to be most convenient.

METHOD

The technique adopted for testing the tuberculin-neutralising potency of the sera was as follows.

The tuberculin dilutions, both test and control, were made up and allowed to stand at room temperature for 48 hours before intracutaneous injection. A 1 in 1000 dilution of O.T. was first made up with normal saline, and to one part of this were added nine parts of the serum to be investigated. As controls, dilutions were made with saline, with sera from people having positive or negative Mantoux tests but otherwise in good health and from patients with diseases unrelated to tuberculosis and sarcoidosis, and with certain animal sera. All the sera were filtered through a Berkefeld N filter candle and tested for sterility before use.

Two intracutaneous injections, each of 0·1 ml., were made on the same arm of each patient, one injection being 1 in 10,000 O.T. made up with normal saline or serum, previously shown to have no tuberculin-neutralising properties, and the other comprising the same amount of O.T. in which the last tenfold dilution was made with the serum to be tested. The tests were read after 48 hours, the diameter of the œdematous area being measured in millimetres.

Sera were obtained from several patients with sarcoidosis. From case 1 (see table I) we were fortunate in getting a large enough quantity for a considerable number of tests to be made, including some with fractionated serum. Other serum came from cases of pulmonary (Boeck's) and cutaneous (lupus pernio or Besnier's

* A report to the Medical Research Council.

Digitized by Google

disease) sarcoidosis, and from a case of Crohn's disease, thought by some to be a manifestation of sarcoidosis.

RESULTS

Tables I–III summarise the results obtained with human sera. From these it is clear that, though the sera from established cases of sarcoidosis are far the most constant in the tuberculin-neutralising test, the phenomenon is occasionally observed with apparently normal sera and in conditions not related to sarcoidosis. Further, serum from a patient with sarcoidosis occasionally does not neutralise O.T., especially after treatment. The test is therefore unsuitable as a routine diagnostic procedure.

A similar neutralisation was occasionally observed with certain animal sera, notably that of the horse. Later work, however, indicates that the neutralisation effected by horse serum bears a close relation to its content of naturally occurring precipitins against tuberculin, which are absent from the specimens of serum we have examined from patients with sarcoidosis.

TABLE I—SERA FROM ESTABLISHED CASES OF SARCOIDOSIS

Case no.	Total skin test	Effect on Mantoux test using 1/10,000 O.T.		
		Complete neutralisation	Reduction by 50% or more	No significant effect
1	22	19	2	1
2	4	3	1	0
3	5	4	0	1
4	4	4	0	0
5	5	3	2	0
6	4	3	0	1
7	5	4	1	0
8	2	1	1	0
9	4	4	0	0
10	4	4	0	0
11 (lupus pernio)	4	3	0	1
Total	63	52	7	4
After treatment:				
12	3	1	0	2
13	3	0	0	3
Total	6	1	0	5

The ability of serum from patients with sarcoidosis to neutralise the tuberculin reaction seems to depend on several factors. First, it seems to vary with the activity of the sarcoid process of the patient from whom the serum is taken. After natural remission of the disease, effective radiotherapy, or surgical removal of the part infiltrated by epithelioid granuloma, there is a pronounced diminution in the tuberculin-neutralising power of the serum. Secondly, when the test was performed on people with progressive tuberculosis, or on guineapigs with active tuberculosis, irrespective of whether the disease was early or advanced, the same serum which had been shown to be effective when injected with O.T. into sensitive persons without active tuberculosis had much less effect.

With so many factors affecting the tuberculin-neutralising power of serum from patients with sarcoidosis, the skin test described above is clearly unsuitable as a routine diagnostic procedure for sarcoidosis. Later work has shown that, at least in some instances, the serum of patients with other diseases having as a pathological feature the mobilisation of epithelioid cells—e.g., kala-azar—may contain a similarly potent tuberculin-neutralising factor (Wylie 1948). This observation is of particular relevance in view of the occasional similarity of the lesions of leishmaniasis to those of sarcoidosis, as first noted by Dupont (1930), and it would be of great interest to know if the serum from cases of berylliosis also possesses tuberculin-neutralising properties, since this condition may be readily confused both clinically and histologically with sarcoidosis (Hardy and Tabershaw 1946, Agate 1948).

TABLE II—SERA FROM DOUBTFUL CASES OF SARCOIDOSIS

Case no.	Total skin test	Effect on Mantoux test using 1/10,000 O.T.		
		Complete neutralisation	Reduction by 50% or more	No significant effect
14	5	3	0	2
15	3	1	0	2
16	3	1	0	2
17 (Crohn's disease)	6	5	0	1
18	3	2	1	0
19	4	2	1	1
20	5	1	0	4
Total	29	15	2	12

DISCUSSION

In view of the ætiological differences between sarcoidosis, leishmaniasis, and berylliosis, these observations suggest that the histological similarity of the lesions of sarcoidosis to those of tuberculosis does not justify the opinion that the former is an atypical form of the latter, especially when other striking differences between the two are evident.

The occurrence of a tuberculin-neutralising factor in the serum in active sarcoidosis, and possibly other conditions, is of considerable interest; and certain features, notably the time required for the reaction to take place in vitro, distinguish this factor from the hypothetical "antikutin" of Pickert and Löwenstein (1908). These workers thought that this substance was present in serum from normal tuberculin-negative persons, but we were unable to demonstrate any such action, thus confirming the observations of Leitner (1942).

Serum from an established case of Boeck's pulmonary sarcoidosis was fractionated electrophoretically by Dr. Alan Kekwick, of the Lister Institute, to whom we express our gratitude. Tests with the various fractions of serum protein revealed that all the tuberculin-neutralising power is in the gamma-globulin, tenfold or even hundredfold dilutions showing considerable neutralising power. Normal human gamma-globulin shows no tuberculin-neutralising power, and the pseudoglobulin and albumin fractions of sarcoid serum possess little or none. In view

TABLE III—OTHER HUMAN SERA

Case no.	Total skin test	Effect of Mantoux test using 1/10,000 O.T.		
		Complete neutralisation	Reduction by 50% or more	No significant effect
Healthy people:				
21 Mantoux −ve	5	0	0	5
22 Mantoux +ve	5	0	0	5
23 Pooled donor serum	4	0	0	4
24 Mantoux −ve	1	0	0	1
25 Mantoux −ve	3	1	0	2
26 Mantoux unknown	5	1	0	4
Total	23	2	0	21
Hospital patients:				
27 Aseptic meningitis	4	2	0	2
28 Perinephric abscess	4	0	1	3
29 Lung abscess	2	1	0	1
30 Diabetes mellitus	3	1	1	1
31 Essential hypertension	3	0	1	2
32 Acute rheumatism	2	0	0	2
33 Ulcerative colitis	5	0	0	5
Total	23	4	3	16

Digitized by Google

of the observations of Salvesen (1935), that in many cases of sarcoidosis there is a proportional increase in globulin with the consequent disturbance of the albumin/globulin ratio, this finding is interesting. It is important to determine whether other conditions exhibiting this phenomenon are associated with the presence of a tuberculin-neutralising factor.

Other properties identified with this factor include its destruction by heat at 65°C for an hour and the failure of soya-bean antitrypsin to affect the tuberculin-neutralising action. The latter distinguishes the factor from fibrinolysin (Macfarlane 1937), which is found in the plasma in conditions of widely differing ætiology. It is noteworthy in this connexion also that, whereas, according to our observations, fibrinolysin neutralised the power of other antigens, such as pollen, to cause a reaction in the skin of a sensitive subject, the tuberculin-neutralising factor of serum from a patient with sarcoidosis did not in any way influence this reaction.

SUMMARY

A tuberculin-neutralising factor is present in the serum of patients with sarcoidosis.

It seems that this factor is present only in certain phases of sarcoidosis.

The sarcoid group of diseases are probably not the only conditions in which this factor may be observed; therefore the test described would be of little value as a diagnostic procedure.

We wish to acknowledge our indebtedness to the clinicians and medical superintendents, too numerous to mention individually, who have helped us in this work.

REFERENCES

Agate, J. (1948) personal communication.
Dupont, A. (1930) *Ann. Derm. Syph., Paris*, 1, 453.
Hardy, H. L., Tabershaw, I. R. (1946) *J. industr. Hyg.* 28, 197.
Leitner, St. J. (1942) Der Morbus Besnier-Boeck-Schaumann. Basle.
Macfarlane, R. G. (1937) *Lancet*, i, 10.
Pickert, C., Löwenstein, R. (1908) *Dtsch. med. Wschr.* 2, 2262.
Salvesen, H. A. (1935) *Acta med. scand.* 86, 127.
Wylie, J. A. H. (1948) D.Phil. thesis, Oxford University.

Preliminary Communication

STREPTOMYCIN-STREPTOKINASE TREATMENT OF TUBERCULOUS MENINGITIS

HISTOLOGICAL sections of the gelatinous material from the base of the brain in patients dying of tuberculous meningitis show an exudate consisting mainly of fibrin, in which tubercle bacilli may be seen. The readiness with which drug-sensitive organisms may be cultured from such material obtained at autopsy after unsuccessful streptomycin treatment suggests that streptomycin cannot penetrate such an exudate. Anything which would facilitate the access of streptomycin to these sheltered organisms seems worthy of trial, and accordingly the possibilities of bacterial streptokinase as an adjuvant to streptomycin have been examined. This substance is a natural product of some strains of streptococcus, and appears to have the ability to activate a naturally occurring profibrinolysin, or plasminogen, to produce fibrinolysin.

MATERIAL AND METHODS

The H64 strain of hæmolytic streptococcus was grown in broth, and the streptokinase so produced was adsorbed on to aluminium hydroxide, washed, and eluted in phosphate buffer, according to a modification of the technique of Tillett and Garner.[1]

The streptokinase obtained by this method has the ability to initiate lysis of a fibrin clot produced either by recalcification or the addition of thrombin to plasma. After experiment it was found that the addition of a drop of thrombin to 0·5 ml. of a 1/20 dilution of plasma from routine blood-sedimentation-rate samples of blood gave a clot comparable to the spider's-web clot which forms on standing in the cerebrospinal fluid from cases of tuberculous meningitis. When streptokinase is mixed with such plasma and a drop of thrombin is then added a clot forms which gradually disappears. By serial dilution the amount of streptokinase necessary to cause clot lysis in 1 hour was ascertained. A hundred times this amount in 1 ml. was chosen as a dose for clinical trial, on the grounds that such a quantity was likely to become diluted approximately a hundred times by cerebrospinal fluid after intrathecal injection in children.

Details of these methods have been published elsewhere.[2] Recently Christensen [3] has published more precise methods of purification and assay of streptokinase.

1. Tillett, W. S., Garner, R. L. *J. exp. Med.* 1933, **58**, 485. Garner, R. L., Tillett, W. S. *Ibid*, 1934, **60**, 239.
2. Cathie, I. A. B. *J. clin. Path.* 1949, **2**, 73.
3. Christenson, L. R. *J. gen. Physiol.* 1947 **30**, 465. *J. clin. Invest.* 1949, **28**, 173.

RESULTS

Intrathecal injection of streptokinase causes a pleocytosis of the same order as that following intrathecal streptomycin. No clinical upset has been observed after its administration. For the past 15 months at this hospital streptokinase has been in regular use in the treatment of tuberculous meningitis, and it has been given intrathecally whenever streptomycin was given by this route. An opalescence appears when streptokinase is mixed with either the calcium chloride or hydrochloride of streptomycin, whereas no opalescence is seen with streptomycin sulphate; consequently only the last salt has been used.

The cases of tuberculous meningitis mentioned here were unselected, ranged in age from 5 months to 12 years, were all bacteriologically proved, and contained the usual proportion of cases of meningitis developing during treatment for miliary lesions. There are two series of cases available for comparison:

Group A.—Fourteen cases treated with streptomycin alone. In these a scheme of treatment was attempted of 4 weeks' daily intrathecal administration followed by a fortnight's rest and then another 4 weeks' intrathecal treatment.

Group B.—Nineteen cases treated with streptomycin and streptokinase. In nearly all these cases intrathecal treatment was carried out every day for 2 weeks, every other day for 2 weeks, and every third day for 2 weeks, streptokinase being given with each injection of streptomycin. The full amount of streptokinase indicated above was given when the dose of streptomycin was 100 mg., and this was halved in the younger children who received 50 mg. of streptomycin.

In both groups, where survival permitted, intramuscular streptomycin (0·02 g. per lb. of body-weight daily) was given for 6 months.

The results were as follows:

	Total	*Recovered*	*Dead*
Group A			
Streptomycin alone	14	3 (*21%*)	11 (*79%*)
Group B			
Streptomycin and streptokinase	19	11 (*58%*)	8 (*42%*)

By recovery is meant a normal cerebrospinal fluid and no signs of active disease. No suggestion of cure is made, as two patients, treated by the group-B régime but not included in the table, relapsed 3 and 4 months respectively after discharge home symptomless and with normal cerebrospinal fluid. The minimum period of treatment and observation is 9 months, and the longest is 23 months.

Of the three survivors in group A, one is mentally defective and one is deaf. Of the eleven survivors in group B, one baby appears to be mentally defective; otherwise no sequelæ have been observed.

Digitized by Google

COMMENT

In spite of the small numbers involved, we have been greatly encouraged by the improvement in our recovery-rate since the introduction of streptokinase, the results obtained comparing not unfavourably with most other published figures. Experience in treating tuberculous meningitis undoubtedly leads to better results, but the disparity in the figures quoted here is too great to be accounted for on such grounds. The combination of streptomycin and streptokinase has the great advantage that it has been possible to reduce the period of intrathecal treatment in most cases to 6 weeks, and this has meant a considerable saving of labour as well as suffering on the part of the patient.

Greater amounts of streptokinase can be given intrathecally with safety than have been used in this group of cases, and the optimum dosage remains to be ascertained.

Fuller details of treatment and results will be assembled later, and this note is published in the hope that other workers may consider a trial of streptokinase as an adjuvant to streptomycin.

The Hospital for Sick Children, Great Ormond Street, London. I. A. B. CATHIE M.D. Lond.

Reviews of Books

Practice of Endocrinology

Editor: RAYMOND GREENE, M.A., D.M., M.R.C.P. London: Eyre & Spottiswoode for *The Practitioner*. 1948. Pp. 366. 52*s*. 6*d*.

THIS book is a valuable addition to British publications on the endocrines. Each section is written by an authority on the subject under discussion, and the book will therefore be one of the most-thumbed volumes in the endocrinologist's library. Seven authors have contributed, under the able editorship of Dr. Raymond Greene, and all write with the background of day-to-day experience, knowing the snags, and aware of the difficulties of recognising, classifying, and managing the conditions described. But however efficient the editing, sections written by different authors are almost bound to be on different planes. In this book the chapters on the pituitary and the adrenals are written by Dr. A. C. Crooke, who has contributed fundamental observations on the histopathology of Cushing's syndrome and adrenal cortical tumours. Since he is primarily a pathologist, his sections in this book are an erudite analysis of clinico-pathological knowledge of these two glands. This masterpiece of exposition will often be quoted; but much of it will be above the average doctor's head—though the book "is intended for general practitioners, most of whom are too busy to concern themselves with unproven hypothesis and academic detail." In the section on the thyroid Mr. F. F. Rundle and Dr. Greene have chosen to be provocative, perhaps rightly, for this subject raises great controversy at present, especially in regard to the treatment of thyrotoxicosis. Their chapter is certainly stimulating, and they have obviously enjoyed writing of conditions with which they have been intimately familiar for years. Whether they have supplied the practitioner with the dogmatic account which he may have been seeking is less certain, though they have certainly revealed much that he probably did not suspect, and given him much food for further thought. The chapters on diabetes by Dr. R. D. Lawrence and on calcium metabolism by Dr. Donald Hunter are simple straightforward practical accounts of two conditions, one common the other rare. They are short and easy to refer to, and they will not let the busy doctor down whatever his dilemma of diagnosis or treatment may be. For these articles alone he would do well to have this book in his possession. The section on sex and reproduction reflects a combination of academic information and practical common sense, while the chapter on adiposity, besides offering some useful tables, is an example of the refreshing literary style of the editor.

Coöperation, Tolerance and Prejudice

A Contribution to Social and Medical Psychology. SAMUEL LOWY, M.D., with an introduction by Robert H. Thouless, PH.D. London: Routledge & Kegan Paul. 1948. Pp. 318. 21*s*.

NO-ONE would maintain today that the subject of Dr. Lowy's book is of only academic interest. By prejudice he understands "bias coupled with an aggressive attitude for which an inadequate reason is given." Such prejudice has been responsible for massacre and torments within the last decade, nor is there reason to hope that tolerance and coöperation are now in the ascendant. Dr. Lowy's experience of psychopathology and social psychology, to which his two previous books testified, qualifies him for the difficult task of examining the roots of prejudice and the means for combating it. He is throughout modest and frank in admitting how incomplete must be his inquiry, and how tentative his conclusions. His reasoning is close, his style lucid, and his breadth of outlook attractive. Although addressed to the expert psychologist and sociologist, the book will be found illuminating by medical and other readers concerned about the dangers that arise from prejudice.

Heart

A Physiologic and Clinical Study of Cardiovascular Diseases. ALDO A. LUISADA, M.D., instructor in physiology and pharmacology, Tufts College. Baltimore: Williams & Wilkins. London: Baillière, Tindall, and Cox. 1948. Pp. 653. 55*s*.

THE first quarter of this book describes the physiology of the circulation and the clinical and instrumental methods of examination. Turning then to the diseases of the heart, Dr. Luisada elects to approach them from an anatomical rather than an ætiological standpoint; thus, aortic incompetence due to rheumatism, syphilis, and other causes is considered under one head, and there is no separate section on syphilitic heart disease; and various congenital lesions will be found in several chapters. The method has advantages, but perhaps more drawbacks. There are short chapters on diseases of peripheral arteries and veins, cardiac drugs, and heart-failure. The style of the book is rather like that of an encyclopædia and it is hard to see how it can meet the needs of the student or any group of the profession. From the mass of unintegrated detail, much of it superfluous, the former will be unable to grasp the first principles of the subject, while a much simpler text would meet the demands of the practitioner. The cardiologist will find something of interest, but more that is not in accord with modern views.

Junior First Aid Manual (British Red Cross Society. 1948. Pp. 66. 2*s*. 6*d*.).—This is a technical presentation of basic first-aid. The bold line drawings aided by contrast colour are clear and well done (but there is a slip on p. 37 where the œsophagus and trachea are confused). It is certainly a useful little book for teaching boys and girls.

Infra-Red Irradiation (3rd ed. London: H. K. Lewis. 1948. Pp. 161. 8*s*. 6*d*.).—Dr. William Beaumont says that his book has been written "for those who have only a superficial knowledge of physics or the sciences on which medical treatment is based"; but it is a little difficult to know for whom it is really designed. He describes the physical basis and physical effects of infra-red irradiation, giving his own technique and making but scant reference to the modern methods of measurement. The most interesting chapters are those devoted to the results of his own clinical experience.

The Premature Baby (2nd ed. London: J. & A. Churchill. 1949. Pp. 167. 12*s*. 6*d*.).—Dr. V. Mary Crosse has revised her famous little book and brought it up to date, especially as regards statistics. Other new matter is to be found, notably in the section on feeding, which is now more definite about what should be done, instead of what might be chosen. Brandy in drop doses still appears twice in the book as a stimulant. Evidence in the popular press, when premature babies are reported as being "fed on brandy," suggests that this is a lethal weapon, and if Dr. Crosse agrees it would be helpful if she would say so unequivocally. She can again be congratulated on her first-class results with a numerically important section of the community.

Digitized by Google

THE LANCET

LONDON: SATURDAY, MARCH 12, 1949

The Cuts

THE cuts made by the Minister of Health—or by the Treasury—in the hospital estimates for 1949–50 have been received in many quarters with consternation. No official statement has been made, but it seems that the estimates submitted by the regional hospital boards have been reduced by about 10%, and the estimates of the teaching hospitals by amounts varying from £25,000 in the case of Addenbrooke's to no less than £300,000 in the case of St. Bartholomew's. It is said that the teaching hospitals have been informed that they must also arrange for the effects of any increases recommended by the Spens Committee to be met out of the reduced estimates; and these increases are likely to be substantial. At first blush the cuts appear to be arbitrary, and it seems a pity that the Minister has not anticipated public reaction by some explanation of the basis on which they have been made.

Since the appointed day the hospitals have admittedly had a very free hand. The Minister has, wisely, relied on their discretion, and for the first nine months of the National Health Service there has been scarcely any check. Hospitals were told to carry on and to submit a budget for the year as from April, 1949. It is not surprising that many of them have taken advantage of their opportunity; they have enjoyed a sense of release from financial restraint which is quite new to them, for the need for economy always weighed heavily on both voluntary and local-authority hospitals. War-time arrears of decoration, renewal of equipment, and restocking of all sorts of domestic supplies have been undertaken on all sides. Such expenditure has, however, been dwarfed by the mounting bills for salaries imposed on the hospitals by the central negotiating machinery established during the war. The revised scales of salaries for nurses and of wages for all categories of domestic staff have altered this part of the hospital budget out of recognition, and the full impact of the payment of medical staff has yet to make its weight felt. In forecasting for 1949–50 hospitals have no doubt allowed for a further rise in the graph, and would be foolish indeed had they not done so. It is therefore perhaps fair to say that the expenditure of every penny has not been scrutinised with the care of pre-war days. On the other hand, there have been few signs of extravagance. Judged from the standpoint of the development of hospital services as envisaged when the National Health Service Act was before Parliament, there may be room for a little pruning here and there, but that is all.

About 60% of the expenditure of a large hospital goes on salaries and wages and is therefore to all intents and purposes fixed. Of the remainder a large proportion is accounted for by such items as provisions and medicines of one kind or another. Nobody would suggest that the hard-won increases in numbers of nurses and domestic staff should be light-heartedly sacrificed, and he would be a bold man who would suggest that there is much scope for saving in hospitals on the cost of provisions. When therefore the Minister urges that the patients' interests must not suffer it is difficult to see where the cuts are intended to fall. Some may be tempted to urge that administrative charges must be reduced; but this is too facile altogether, for the administration in a hospital represents a very small proportion of the total cost, and any ill-judged "economies" here would be likely to have a disastrous effect. Hospital administration is becoming increasingly important and needs to be a career attractive to able men.

The principle—on which the Minister has been insistent from the start—that the hospitals should be financed by round-sum allocations, and left to use the money as they think best, is sound enough so far as it goes. But if the estimates sent in are going to be pruned at all there must be in the background some system of checking comparative costs; and it seems important that this should be, and be known to be, as fair a check as is humanly possible. In the hospital world, statistics based on comparative costs per occupied bed and outpatient attendances have been known and used for many years; and the merits and defects of the system are pretty well understood. For some time past the King's Fund and others have been advocating the development of a more modern system of departmental accounting in hospitals. The Ministry has quite rightly decided that the time is not yet ripe for the general introduction of such a system. If, however, small groups of comparable hospitals could be costed departmentally, adequate data could surely be obtained to ascertain *units of cost on the basis of the service rendered by each department* as contrasted with the all-in cost per occupied bed. Such results could be published and used as a measuring-rod when the estimates coming in from the hospitals have to be criticised or justified to the Treasury. The plan need in no way conflict with the primary principle that a hospital should have a free hand to spend the total sum thus calculated; what they save on the swings they can spend on the roundabouts.

Meanwhile it may be that the Minister will have to think again, and agree to reconsider some of the more spectacular cuts as their consequences become apparent. But we are still too much in the dark as to the considerations which have guided his action to warrant us in arriving at any hasty conclusions.

Treatment of the Infected Hand

THE number of man-hours lost from infections of the hand is quite staggering. It is no longer true, however, that these cases are usually left to a junior resident, for most enlightened hospitals now make special arrangements for their care. Within the last few years several considered reports on the results of treatment have appeared; and on another page we publish one from the Birmingham Accident Hospital by Mr. STEWART HARRISON and his colleagues.

This account is concerned chiefly with the value of systemic penicillin in finger-pulp infections. Penicillin's reputation in this field has been inconstant. Its dramatic effect on infections elsewhere in the body

Digitized by Google

fostered the hope that it would bring about great improvement in infections of the hand; but this hope has been only partly fulfilled, and some even say that it has little, if any, beneficial effect.[1] At first penicillin was used locally, in the form of a cream, as a supplement to surgery. Administered in this way it could hardly be expected to have any potent action; yet most observers are satisfied that application—either with a cream, or with a fine dusting or insufflation of the powder—is well justified. But attention is now turning to systemic injection, in the hope that radical surgical procedures may be modified or even avoided. The dose is being stepped up, and now an initial injection of 500,000 units, followed by 1,000,000 units a day for five days, is quite commonly used. A glance at the figures in table II of the article in this issue shows the progressive improvement in healing-time with increasing doses. Here an attempt has been made to judge the issue dispassionately, by selecting as far as possible comparable cases—i.e., pulp infections—some to be treated with penicillin and some without. In any clinical investigation it is difficult to get exact controls, but great pains have been taken to exclude the many variables. "Healing-time" has been used as an index for comparison, though even this must be difficult of definition and interpretation. The healing-time improves progressively in both groups of cases, the best results being obtained, strangely enough, in certain out-patients. Could it be that these were milder cases? It is also shown that minimal incisions produce better results than the J-shaped incision so often used. By an ingenious device, finger volumes were recorded, and it has been found that increase in volume of 12% indicates the presence of pus and the need for surgery.

The Birmingham workers believe that delay in operation increases the risk of complications. PILCHER et al.[2] advised a rather more conservative attitude, though they suggested cautious incision directly over the abscess (heeding the lines of Langer) when pus is formed. PILCHER holds that tissue death is due to exotoxins from the *Staphylococcus aureus*—which is responsible for some 85% of these infections—rather than to tension as was postulated by KANAVEL.[3] If this is so, immediate operation would not seem essential; and penicillin, though it cannot be expected to reverse the pathological process, ought to be able to prevent its spread—which it appears to do. Operation will nevertheless be required in all but a small proportion of cases; and minimal incision, carried out under full anæsthesia, with a tourniquet,[4] and with care and deliberation, is to be commended: there should be little need to stress the folly of imperfect incision under an ethyl-chloride spray. LOUDON and his associates[5] at Oxford have reported excellent results with slightly more extensive incisions and primary suture or early skin covering, after 24 hours' preoperative preparation with penicillin and vitamins. This would seem a further step forward, but the method can be advised only in a well-ordered clinic. All authorities agree on the value of infrequent dressings, elevation, and immobilisation till resolution takes place.

There can be no doubt that in the past decade the fate of infected hands has greatly improved, owing partly to segregation of cases into special clinics, and partly to the advent of penicillin. But the selection of cases for surgery, the exact timing of the operation, and the technical details of it are still subjects for debate.

1. Bolton, H. Catchpole, B. N., Jepson, R. P. *Lancet*, 1947, ii, 608.
2. Pilcher, R. S., Dawson, R. L. G., Milstein, B. B., Riddell, A. G. *Ibid*, 1948, i, 777.
3. Kanavel, A. B. Infections of the Hand. Philadelphia, 1940.
4. Eckhoff, N. L. *Lancet*, 1931, ii, 343.
5. Loudon, J. B., Miniero, J. D., Scott, J. C. *J. Bone Jt Surg.* 1948, **30B**, 409.

Infected Air

ACUTE respiratory infections account for 40–60% of sickness absence from work and school. Our knowledge of the sources, modes of dispersal, and vehicles of the infecting agents, and indeed of the infecting agents themselves, is still very imperfect; and direct droplet infection may not be as important as we used to think. Bacteriological and epidemiological studies indicate that the infective material from many respiratory infections pollutes the air, either as droplet nuclei which remain suspended in the air for variable periods, or as infected dust particles which are raised into the air during various activities. If bacterial air pollution is shown to be correlated with the risk of respiratory infection, reliable methods of measuring the degree of pollution can be brought into use; a bacterial standard of aerial cleanliness can be adopted, and methods for purifying indoor air can be developed with the prospect of reducing morbidity.

In the early days of the 1939–45 war a team of scientists at the National Institute for Medical Research set out to solve some of these problems. Much of the work has already been published, but a mass of useful information, resulting mainly from the investigations of R. B. BOURDILLON, O. M. LIDWELL, and J. E. LOVELOCK, has now been collected under one cover.[1] These studies fall into four main groups: (1) methods of air sampling and of testing the efficiency of air disinfectants; (2) methods of disinfecting air and the conditions determining their effectiveness; (3) measurements of bacterial pollution of the air in factories, hospitals, operating-theatres, naval vessels, &c.; and (4) experimental studies on the transmission of airborne infection in animals. For measuring contamination of the air by bacteria-carrying particles, increasing use is being made of the slit sampler, with which air is drawn at a fixed rate through a slit, to impinge on a rotating plate of solid culture medium. American workers prefer either the Wells air centrifuge—somewhat similar in principle to the slit sampler—or broth samplers, in which the airborne particles are collected in a fluid medium after impingement and atomisation on a moist glass surface. While broth samplers are easier to produce and to transport, the slit sampler is more convenient, since as many as 80 two-minute samples can be taken in a morning; and sudden changes in bacterial contamination can be accurately recorded, as BOURDILLON and LEONARD COLEBROOK found when studying the liberation of bacteria during wound dressings. Moreover, when sampling on to a

1. Studies in Air Hygiene: by R. B. Bourdillon, O. M. Lidwell, and J. E. Lovelock; with W. C. Cawston, L. Colebrook, F. P. Ellis, M. Van Den Ende, R. E. Glover, A. M. MacFarlan, A. A. Miles, W. F. Raymond, E. Schuster and J. C. Thomas. *Spec. Rep. med. Res. Coun., Lond.* no. 262. London: H.M. Stationery Office. 1948. Pp. 356. 7*s*. 6*d*.

Digitized by Google

solid medium, the mean size of the bacteria-carrying particles can be roughly estimated by comparing the colony count with the total numbers that settle on an open petri dish. The slit sampler is also remarkably constant in its performance. On the other hand, a broth sampler may be preferred when bacterial contamination is heavy, or when bacterial clusters have to be broken up; though even here it is generally more useful to know the size and number of bacteria-carrying particles than the total number of contained bacteria.

Many methods may be pursued in an attempt to keep indoor air clean. Thus masks and handkerchiefs may be used to control dispersal from the respiratory tract, and dust-suppressive measures to prevent dissemination of infective material from floors and fabrics. Natural or mechanical ventilation dilutes and replaces dirty air with clean air, while daylight and sunlight (even through ordinary glass) are good bactericides whose effectiveness may be supplemented by ultraviolet light. Large volumes of air can be completely sterilised by passage through a hot pipe or furnace at a temperature around 350°C; or the air may be cleaned by electrostatic precipitation—a method used more often for dust control than for obtaining bacterial purity. Lastly, certain chemical substances when finely sprayed or vaporised act as powerful aerial bactericides.

In the present studies attention has been paid to most of these methods, and particularly to the chemical disinfectants. These substances are now believed to act by condensing, from the vapour phase, on the bacteria-carrying particles, which are assumed to be equivalent to a watery solution in equilibrium with the water vapour in the air. If this is the explanation, bactericides most effective at moderate or low humidities will be those that have a high bactericidal power and rapid killing-rate in aqueous solution, and also have a low vapour pressure and a high solubility in water. But additional requirements must also be met: the substance must act on both moist and dry bacteria-carrying particles at prevailing humidities and temperatures; it must be free from toxicity, irritation, odour, and corrosiveness; it should be easily vaporised; and its cost must be low. Chemicals fulfilling some or all of these requirements include sodium hypochlorite (forming hypochlorous acid), propylene and triethylene glycol, lactic acid and other α-hydroxy-acids, resorcinol, and hexylresorcinol. Sodium hypochlorite is efficient, cheap, and easily available if needed for use on a large scale; it is usually atomised by a special spraying machine. Triethylene glycol is remarkably effective in very low concentrations, and is neither irritant nor toxic; but for maximum efficiency it needs relatively high humidities. Lactic acid is active in drier atmospheres, but is irritant if used much above its proper concentration. Another member of this family, α-hydroxy-α-methylbutyric acid, called C-acid for short, is less irritant and has the great merit of vaporising at room temperature. Resorcinol is suitable for single or intermittent short periods, but its rapid disappearance after vaporisation makes it less satisfactory for continuous use. Indeed the main difficulty with most aerial disinfectants, under field conditions, is to maintain an adequate concentration when ventilation is variable, and when they react with dust or condense on surfaces. A further disadvantage is that these substances are less effective against large dry bacteria-carrying particles than against smaller moist particles; which means that where dust-borne infection is a hazard the efficiency of disinfection may not be high.

This last drawback applies also to ultraviolet light, which, unlike the chemical bactericides, acts better in a dry than in a moist atmosphere, but which must be restricted to an irradiated "ceiling" at a height of 7 ft. or more, or to "curtains" of light instead of doors or partitions. Ultraviolet radiation is clean, safe, free from toxic effects, and easy to maintain; but installation and maintenance costs are considerable. Its efficiency as an aerial disinfectant depends on care in placing the lamps, keeping them clean and bactericidally effective, and ensuring a good rate of vertical circulation of the air, and the use of ultraviolet light should if possible be combined with dust-suppressive measures. Indeed, prevention of the dissemination of dry infective particles from floors, bedding, handkerchiefs, and clothes is likely to prove one of the most practical steps towards control of airborne infections.

Hæmoglobinuria

To the patient, whether he thinks himself well or knows himself ill, the passage of hæmoglobin in the urine is a dramatic and alarming event. In young adults it may occur after strenuous marching or other exercise, and three typical examples of this "march hæmoglobinuria" are described by LUBRAN and SAKULA in our present issue. People who develop it are abnormal in that they have a low renal threshold and may excrete hæmoglobin in the urine when the free hæmoglobin in the plasma is as little as 25 mg. per 100 ml. LUBRAN and SAKULA's cases showed this low renal threshold for hæmoglobin, and they also conformed to the remarkable condition that the exercise must be taken in an upright position; violent and exhausting efforts made when lying down had no effect. To explain this phenomenon, LUBRAN and SAKULA suggest that a contracting spleen ejects into the circulation red blood-cells rendered unduly fragile by lingering in the splenic sinuses; when the patient lies flat, they say, splenic contractions are reduced and there is therefore no free hæmoglobin in the blood. But they do not make this explanation any easier to accept by their observation that march hæmoglobinuria did not appear when the subjects had been given ascorbic acid to saturation point. This preventive effect has not always been found by others, but Service doctors may find ascorbic acid worth a trial.

In the incidents followed by march hæmoglobinuria little blood is hæmolysed; but in the severer forms of hæmoglobinuria there is nearly always an associated anæmia of hæmolytic type. Analysing this association STATS, WASSERMAN, and ROSENTHAL [1] recognise four types seen "in general civilian medical practice in temperate climates": (1) the Marchiafava-Micheli syndrome (paroxysmal nocturnal hæmoglobinuria), (2) hæmoglobinuria due to cold agglutinins, (3) hæmoglobinuria due to drugs, and (4) the "idiopathic" type. They are at pains to emphasise the difference between hæmolytic anæmia with and without hæmoglobinuria; for they believe that

1. Stats, D., Wasserman, L. R., Rosenthal, N. *Amer. J. clin. Path.* 1948, 18, 757.

Digitized by Google

patients with hæmoglobin in the urine are unlikely to benefit from splenectomy.

In the Marchiafava-Micheli syndrome there is a persistent hæmoglobinæmia, and spectroscopic examination of the blood plasma (taken without hæmolysis) reveals oxyhæmoglobin always and methæmalbumin sometimes. In suspected cases it is important to examine the blood plasma in this way because, as HAM and HORACK [2] pointed out, hæmoglobinuria may be transient and infrequent, and, especially in women, may be missed altogether. Another distinguishing feature of the Marchiafava-Micheli syndrome is persistent hæmosiderinuria; and the condition may be detected by special serological tests like the spontaneous hæmolysis of clotted blood at 37°C [3] and HAM's acid hæmolysis test.[4]

Hæmoglobinuria caused by cold agglutinins is brought on by local chilling of exposed parts; an unusually detailed account of such a case was given by L. K. MALLEY and M. D. HICKEY in our last issue. The affected patients sometimes have other symptoms related to temperature changes, such as Raynaud's phenomenon. Cold agglutinins are sometimes found in other anæmias; but hæmoglobinuria from this cause differs from the Marchiafava type because it can be detected only during the hæmolytic phases, because hæmosiderinuria is absent, and because the special serum tests are negative. STATS and WASSERMAN [5] have described a special test in which the blood hæmolyses rapidly on shaking in the cold.

The drugs most often responsible for hæmoglobinuria are the sulphonamides. STATS, WASSERMAN, and ROSENTHAL [1] record cases due to sulphanilamide, sulphapyridine, and sulphadiazine. Phenylhydrazine has also been implicated. The plasma from these patients often contains very little oxyhæmoglobin, but it gives a positive Schumm test for methæmalbumin.

In the fourth or idiopathic group are acute hæmolytic anæmias in which hæmoglobinuria follows the sudden intravascular hæmolysis of considerable amounts of blood. They respond to blood-transfusion and rarely relapse.

In treatment STATS, WASSERMAN, and ROSENTHAL favour repeated blood-transfusion. In hæmoglobinæmia with hæmoglobinuria, they hold, splenectomy is inadvisable, even when the hæmolysis is so severe that the hæmoglobin level in the blood is dropping in spite of transfusion. Stored blood can be used even for patients with cold hæmagglutinins. Reactions are especially likely in the Marchiafava-Micheli type, and for such patients the amount of blood should be kept to the minimum necessary to stop the hæmoglobinuria and keep the blood hæmoglobin from falling too low. They usually recover satisfactorily and maintain a fair level of hæmoglobin. In this connexion the observations that J. V. DACIE and P. L. MOLLISON recorded in our last issue are of special interest. In a case of this kind they found that most of the red blood-cells were unusually sensitive to the normal hæmolysins of plasma, but there were also some relatively insensitive red cells. The patient's hæmoglobin level may depend on the relative proportion of these insensitive cells.

The lessons to be learned from all this are that patients with hæmoglobinuria must be carefully investigated by special techniques that are apart from normal routine, and that we should use the spectroscope more often to look for persistent hæmoglobinæmia. Thus we may be able to distinguish more certainly the patients with hæmolytic anæmia who will not respond to splenectomy.

2. Ham, G. C., Horack, H. M. *Arch. intern. Med.* 1941, **67**, 725.
3. Hegglin, R., Maier, C. *Amer. J. med. Sci.* 1944, **207**, 624.
4. Ham, T. H., Dingle, J. A. *J. clin. Invest.* 1939, **18**, 657.
5. Stats, D., Wasserman, L. R. *Arch. intern. Med.* 1943, **72**, 506.

Annotations

TOWARDS A NEW DEAL

THE Conference of Local Medical Committees met last week in special session to consider what action should be taken to improve the remuneration of the general practitioner. As text for the conference, the General Medical Services Committee had prepared a report suggesting that in view of the changes in the cost of living and of practice expenses the total monies allotted to the general medical services were insufficient. This had had a serious effect on the incomes particularly of the doctors who practise in areas where the average size of practice list is low. Expert guidance had been sought on money values, and a case was presented for the conference to criticise before it was taken to be argued with the Ministry of Health and the Treasury.

Criticism came in plenty. All the delegates thought that more money is needed, but only after long debate did they agree on the total sum that should be asked, and the use to which any increase received should be put.

The earliest conflict of opinion arose because the General Medical Services Committee proposed asking for a betterment figure of 170%, though expert opinion suggested that the proper equivalent of £100 of income in 1939 is £185 today. Some delegates felt that to abandon the figure of 185 before negotiations began would jeopardise all chance of a settlement that could satisfy the needs of the profession. Though few seemed confident that so large a betterment figure could be granted in present economic circumstances, many still insisted it was the figure to which the doctor was entitled, and the lowest point from which bargaining could start. The chairman of the committee, on the other hand, held that nothing would be lost by making the more reasonable demand. In any negotiations our representatives would have to take into consideration not only the change in money values but also the expectation of income in comparable professions: for the figure of 170 they would have a strong and arguable case, and every opportunity to maintain that the demands were not unreasonable. As the debate progressed the conference was won to this point of view; the calculations presented in the committee's report were accepted, and the Ministry will be told that the present total annual remuneration for the general practitioner falls short by some £16½ million of that which is really needed if the expectations of income raised by the Spens recommendations are to be fulfilled.

The conference then considered what would be the most equitable way of distributing any new money obtained from the Government for general practice. As everyone now sees, the doctors whose income has been most reduced by the Act are those with static small lists practising in areas where little change in the size of a practice can be expected, at least until death or retirement changes the doctor population of the neighbourhood. The financial handicap under which these men work would not be removed if the new money were translated into a universal increase in the capitation fee; and as the arguments in the conference developed it became clear that the solution most acceptable was the graded capitation fee. The General Medical Services Committee had themselves reached this conclusion, and had argued that all the new money received should be devoted solely to augmenting the capitation fees paid on the first thousand patients on each doctor's list. The conference gave assent.

So now, having stood the test of a gruelling day's debate, the committee's report goes forward unchanged in the smallest detail. A policy has been propounded

Digitized by Google

and accepted which will deserve, when it reaches Whitehall, the most sympathetic consideration. Besides giving appreciable relief to the doctors with small lists whose need is greatest, the suggested loading of the first thousand capitations would encourage their more heavily burdened colleagues to limit their lists and to provide much-needed openings, as assistants or partners, for would-be entrants to practice. The country then might count on gaining, in return for its additional expenditure a service more efficient than the present.

NEW HOPE FOR THE OLD

THE Chinese reverence for age has much to recommend it, for it ensures care and respect in later life. We in this country have been roused somewhat late to the plight of many of our own old people, and much remains to be done for them. Many who are ill are still denied the hospital beds they need, and interim plans are being made to tide them over their difficulties—for example, those mentioned at a meeting reported on p. 462.

The National Corporation for the Care of Old People, founded in 1947 by the Nuffield Foundation and the Lord Mayor's National Distress Fund, have now described their first year's work.[1] Grants to the value of £257,620 have been made to voluntary bodies starting homes for old people; and it is pleasant to note again that the corporation favour small homes of 25–30 residents. They are also ready to encourage the founding of rest-homes, perhaps linked to certain hospitals, whither old people now occupying hospital beds could be transferred as soon as they no longer need treatment; but they rightly point out that, unless the beds thus released were filled again with old patients only, this procedure would not serve their purpose. The people of South Africa have made the handsome present of £1 million to the people of Great Britain, to be used for certain objects; and an allocation of £170,000 made to the corporation has been set aside for the provision of rest-homes for the infirm, short-stay or holiday homes, and non-residential clubs in various parts of the country. By their use of this gift the corporation hope to prove that a properly integrated system based on a geriatric unit in a hospital will help to solve the problem of the aged sick, and to prevent much unnecessary ill health among the old. A property to be used in this way has already been bought on the banks of the Clyde. An advisory service is being set up and has already done good work. On the advice of the corporation a redundant hospital in Durham is to be converted to receive 40–50 old people, including 15 in need of care and attention though not necessarily of nursing. Except for this infirm group, the old people will live in single rooms or flatlets, and there are to be communal dining, sitting, and recreation rooms. The corporation has also encouraged the employment of old people in occupations suited to their capacity. Grants have already been made to help in the employment of old men in rug-making, and on a fruit farm in Durham. In an attempt to assess the costs of setting up and running homes the corporation are circulating a booklet to voluntary bodies suggesting some standard methods of accounting. The use of these, they say, would greatly simplify the task of collecting and issuing figures on present-day costs.

One of the many hopeful projects now in view is the establishment by University College Hospital of a large unit for the aged and chronic sick in the old St. Pancras Hospital which now forms part of the U.C.H. teaching school. Lord Amulree, of the Ministry of Health, who has done so much to arouse interest in the better care of the aged, has been appointed physician to University College Hospital with charge of this unit.

1. From the corporation at 9, Mecklenburgh Square, London, W.C.1.

HEALTH CENTRES

SOME of the unanswered questions regarding health centres were discussed last Monday by the section of epidemiology of the Royal Society of Medicine. As an architect, Mr. W. J. Durnford advised flexibility in design; for here was a problem without precedent in this country. One of the questions he asked was which units should be relegated to an upper floor; should the minor-operations room be upstairs, or ought it be placed on the ground-floor and some of the practitioners work above? Furthermore, should the approach be by a single entrance to a single waiting-room or by multiple entrances to multiple waiting-rooms? He warned his hearers that adaptation was costly and the results seldom satisfactory; and he was equally glum about techniques of rapid erection.

The potential advantages of the health centre were reviewed by Dr. Talbot Rogers, chairman of the B.M.A. committee which has been considering this subject. Among the benefits he enumerated were the opportunity for consultation and mutual aid, the promotion of friendly competition, and the opening for the old to teach the young and for the young to rejuvenate the ideas of the old. In a field survey the committee had found that partnerships were better equipped than one-man practices, and they were often more popular with patients. An institutional atmosphere should be avoided; the centre should not be modelled on the lines of a local-authority clinic. Since attendance would be sporadic, health education by progressive exhibitions would not be feasible; and anyhow the consulting-room should not be made into an exhibition hall. A case could be made against including full pharmaceutical services; but the advisability of inclusion could be decided only by experience. Radiological and major pathological investigations and physiotherapy would best be conducted from hospital, provided this was reasonably near; the centre should contain a side room, and in the past year it had become evident that pathologists would be able and willing to undertake examinations for the practitioner. On the whole he thought that no night accommodation was necessary for the doctor on duty, provided the centre's caretaker was competent. The present need was to provide means whereby the practitioner could absorb the extra load imposed by the new service; and this relief could be afforded only through centres. The construction of one centre had been approved; this was scheduled for completion in two years, and a further five might elapse before its effectiveness could be judged. Were seven years to pass before it was decided whether and how centres were to be multiplied?

Dr. Frank Gray abjured forced development; practitioners should enter the centre willingly—and in partnership. He thought that at the centre two committees would be formed; the practitioners would form a committee naturally, and the local health authority instinctively; there would also probably be an intermediate body representing the local health authority, the executive council, the local medical committee, and those working at the centre.

From experience at Finsbury, Dr. C. O. S. B. Brooke concluded that in London some people would be unwilling to travel even one mile to a centre; and, he added, patients did not relish sitting in a single, common waiting-room.

Dr. H. C. Boyde complained that the subject was being considered out of its context; the need was urgent. Fundamentally the new strain was being borne by the practitioner, who was now sometimes unable to gain admission to hospital of acutely ill patients. Since July 5 the quantity of medical service had increased, but not the quality; for better quality centres were

Digitized by Google

essential. The real question was one not only of bricks and mortar but of personalities—namely, how different outlooks and temperaments were to be integrated in the centre. Surely, this being so, the right course was to begin experimentation now, even if the buildings were not highly desirable; "Let us go back to adaptation with all its defects." In West Ham he was participating in a plan for a health centre in a building that could be adapted in three or four months at a low cost in money and steel. So far as he could tell, the official approach was the very reverse of urgent.

Dr. J. A. Scott held that a good start was necessary; to begin in a small way might antagonise opinion. Sir Allen Daley, the president, observed that speakers had made little mention of the most important user—the patient.

THE UNDESCENDED TESTICLE

AT Great Ormond Street and at the Boston Children's Hospital the endocrine treatment of undescended testicle is never used. Mr. Denis Browne opened a discussion at the section of endocrinology of the Royal Society of Medicine on Feb. 23 with this rather startling statement. He went on to say that three-quarters of the undescended testicles present before puberty are high or low retractile cases which will descend spontaneously; chorionic gonadotrophin will accelerate their descent but will not bring down testicles that would not descend spontaneously. In operating to bring down testicles which are ectopic or are otherwise prevented from descending it is of cardinal importance to avoid any tension on the pampiniform plexus of the cord, for tension causes reflex vasoconstriction and later atrophy of the testicle. The testicle should be freed and placed in the scrotum, but in Mr. Browne's view should not be tied to the thigh or pushed through to the opposite side of the scrotum. Dr. T. Svend Hansen, from Denmark, discussed his fertility studies [1] on operatively treated and untreated cryptorchidism. In 30 patients with bilateral undescended testicles 52 testicles were brought down by operation; subsequently only 11 were anatomically normal in position, size, and consistence. Out of 25 of the patients submitted to semen examinations 14 were presumably sterile; in 4 fertility was severely impaired, in 2 moderately impaired, in 3 slightly impaired, and in 2 apparently unimpaired. These figures seem to imply that a functionally normal result was observed in something like a fifth of the cases operated on. Svend Hansen rejected MacCollum's finding [2] of fertility in 11 of 15 patients operated on for bilateral undescended testicle as based on insufficiently thorough examination of the semen. In unilateral cases, he has found that cases operated on show no advantage in the sperm test over those left alone. Dr. Harold Engberg, reporting his findings on hormone excretion, said that men who have had undescended testicles show the same level of androgen excretion—more than in castrates but less than in normal men—whether they have been treated by operation or not. From Dr. Engberg's work and his own, Dr. Svend Hansen concluded that operation is unsatisfactory as regards the production of fertility, and he recommended that surgical measures should be used conservatively. As Dr. H. Gardiner-Hill, president of the section, pointed out that, until fertility studies have been reported on cases treated with chorionic gonadotrophin it is difficult to assess the significance of Svend Hansen's work. It would also be desirable to find out the late functional result where testicles have descended spontaneously at puberty, for Cooper [3] suggested twenty years ago that the testicle which remains undescended after the age of 3 years undergoes degenerative changes. Though Mimpriss [4] maintained that the observed changes are due to failure to develop, rather than to degeneration, Dr. P. M. F. Bishop in the discussion drew attention to Cooper's work as important.

No further new work was reported at the meeting, and the views expressed are covered in Dr. Bishop's review [5]; but some of the emotional aspects of this problem are worth considering more fully. A disadvantage of endocrine therapy which Mr. Browne emphasised is that the penile enlargement may embarrass the young boy. Dr. Bishop thought this uncommon and that such troubles as precocious masturbation and heterosexual advances are rare. It is well to remember that surgical operations in children are apt to be followed by nightmares, increased dependency, and other psychological disturbances, and operations on the genitals seem more likely to lead to upsets than operations on other organs. But if hormone and operative treatment have their emotional sequelæ so has "masterly inactivity," for the consciousness of having only one or no testicles may itself disturb proper development, while parental anxiety from the same cause will have a bad effect on the boy.[6] There are psychological arguments for and against early or late treatment of undescended testicles. If Cooper's views are accepted, treatment will be started at the age of 3–4 years. At this age there is much greater likelihood of upset from surgery, and in the family circle the patient is less exposed to embarrassment from secondary androgenic effects of endocrine treatment. If treatment is postponed until the age of 12 the child will grow up conscious of a defect, but it should be possible to relieve his and his parent's anxiety, and when treatment is instituted he will be able to comprehend its purpose and possible results. In all cases, though steps should be taken to avoid the immediate emotional effects of undescended testicles, we must bear in mind that failure to descend by adult life will have grave results in deficient androgen secretion and sterility.

The unilateral undescended testicle should probably be dealt with as follows. If it is a high or low retractile testicle, the boy and his parents should be reassured. If it is ectopic in the superficial inguinal pouch or elsewhere, it should be operated on at about the age of 9, with chorionic gonadotrophin before and after operation to make the operation easier and the results better. The operative procedure should avoid any tension on the spermatic cord, the cord being freed and the testicle placed in the scrotum with no attempt to anchor it. Where there is no certain evidence of obstruction to descent—for example, when the testicle is thought to be in the inguinal canal—hormone treatment should be started at about 12 years and continued for three or four months, after which if the testicle has not come down recourse should be had to surgery. Where the condition is bilateral there seems to be a greater chance of spontaneous descent at puberty, and in view of the disappointing functional results reported after surgical treatment this should be used conservatively. The ectopic testicle will be treated surgically with endocrine therapy as an aid. When there is no certainty of obstruction, treatment should be postponed till the first signs of puberty appear; chorionic gonadotrophin should then be given in full doses, and if the testicles have not descended after four months' treatment operation should be advised. In bilateral cases where surgery is required for pain, torsion, &c., the smallest operation possible is advisable, so that spontaneous or endocrine-aided descent may take place at puberty. Bilateral hernia associated with cryptorchidism is similarly left if possible until after puberty; unilateral hernia with bilateral undescended testicles should be treated as a hernia.

1. Svend Hansen, T. *Acta chir. scand.* 1946, **94**, 117.
2. MacCollum, D. W. *Arch. Surg.* 1935, **31**, 290.
3. Cooper, E. R. A. *J. anat. Lond.* 1929, **64**, 5.
4. Mimpriss, T. W. *Lancet*, 1938, **1**, 533.
5. Bishop, P. M. F. *Guy's Hosp. Rep.* 1945, **94**, 12.
6. Bruch, H. Advances in Pediatrics. New York, 1948; vol. III, p. 262.

Digitized by Google

These lines of treatment are now widely accepted. But there is a great need for late follow-up reports on the functional results of the various treatments adopted—reports which give the site of the testicle before treatment, the treatment used, and the anatomical and functional results obtained. For only facts will provide the cooler climate in which discussion of this problem, like the organ itself, can be truly fertile.

SEXUAL OFFENDERS

"... in regard to sexual offenders, punishment without treatment is not likely to have a beneficial effect; indeed, it can make these offenders worse, and thus more likely to repeat their offences. In a high proportion of cases imprisonment without treatment may have consequences to the community even more dangerous than to the offenders themselves."

In stating this belief [1] the Joint Committee on Psychiatry and the Law, appointed under the chairmanship of Dr. Doris Odlum by the British Medical Association and the Magistrates Association,[2] will have the support of almost the whole profession. Their opinion can doubtless be substantiated by figures: certainly our present penal system does not prevent recidivism in other types of offence as Mr. Claud Mullins (who was a member of the committee) indicated in his address to the Royal Society of Medicine last year.[3] The committee point out that some, and probably many, sexual offenders can be classed as suffering from mental illness to which the aberrant conduct is related; from character deviation (including cases of people who are mentally normal apart from their sexual abnormality); from gross or slight defect of the intelligence; from moral defect not associated with defect of intelligence; or from physical disorders (such as cerebral arteriosclerosis or endocrine changes). The group of character deviations includes the cases of inversion and perversion, some of which are amenable to treatment. The numbers of offenders who fall under one or other of these headings are sufficient, the committee hold, to warrant special provision being made for them. As regards homosexuals, they think there may be a good case for bringing English law into line with that in most European countries, where the law does not concern itself with homosexual conduct in private between consenting adults. Apart from the difficulty of enforcing them, laws penalising such conduct offer encouragement to blackmail. (The anxiety and prejudice which homosexuality is apt to excite probably has its roots in painful repressed memories.) Psychiatrists regard homosexual behaviour as evidence of a pathological state which may well be amenable to treatment—an arrest of the emotions at less than adult level. Mere punishment, and particularly imprisonment (which places the offender in a purely homosexual environment) is unlikely to result in cure; indeed the committee were concerned to find how many of those found guilty of any sexual offence are sent to ordinary prisons, probably in most cases without treatment.

Nevertheless they regard it as important to establish guilt where it exists. Juries are often unwilling to convict in these cases, either because they are loth to believe the facts or because they do not appreciate their gravity for the victim. It is seldom in the offender's best interests to acquit him; he needs treatment, and often this might best be given, the committee believe, in "special institutions" such as those recommended in the East-Hubert report.[4] These would be within the prison service and would provide residential psychiatric treatment where offenders needing it would be obliged to stay for a period. The Home Secretary should have power, the committee think, to discharge offenders, regardless of the length of their sentences, when they could safely be set at liberty. They are opposed to short-term sentences, which give no time for curative treatment and are ineffective as a deterrent.

To protect children from the strain imposed by waiting months to give evidence about offences committed against them, and from the rigours of cross-examination, the report proposes that such cases should be tried at juvenile courts, or else at assizes or quarter sessions by the presiding judge, recorder, or chairman, assisted by two magistrates experienced in juvenile court work. When a sexual offender has been convicted the court should be obliged to seek the advice of a duly qualified medical practitioner, or better a team such as that used in child-guidance clinics. If evidence on the mental health of the prisoner is needed during the trial, a psychiatrist should be called, not by the prosecution or defence, but by the court, and should be open to cross-examination by both sides.

The report as a whole is temperate, and should appeal to all who wish to see criminal procedure in these cases brought into line with modern knowledge.

1. The Criminal Law and Sexual Offenders. Report of the Joint Committee published by the British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1. Pp. 24. 3d.
2. The medical members of the committee were Dr. ODLUM, Dr. F. BODMAN, Dr. DENIS CARROLL, Dr. R. G. GORDON, Dr. J. G. THWAITES, and Dr. W. G. JOHNSTON.
3. See *Lancet*, 1948, ii, 816.
4. The Psychological Treatment of Crime. By W. Norwood East and W. H. de B. Hubert. London, 1939; see *Lancet*, 1939, i, 583.

CANCER OF THE BREAST

IN 1938–39 the clinical cancer research committee of the British Empire Cancer Campaign began a clinical survey of all cases of cancer seen in London hospitals. These included 2529 cases of cancer of the breast, which have now been followed up for five years or more. A report on the findings [1] shows that a lump in the breast was the first complaint in 77·4% of the patients; pain was the first complaint in 11·6%, discharge from the nipple in 2·2%, and symptoms due to metastases in 1·6%. In 1·6% the tumour was discovered by the doctor or during routine examination, having caused no symptoms. Of all the patients 44·1% consulted a doctor within three months of noticing the first symptoms, and 15·3% during the next three months; in 33·3% the symptoms were of more than six months' duration before advice was sought. Of those consulting a doctor 85·6% were referred to hospital at once, but 3·6% were told that the condition was not serious and 4·8% received palliative treatment for more than six months.

Among 703 patients treated by radical mastectomy alone, the average five-year survival-rate of traced cases was 47·6%, ranging from 68·2% of those in stage 1 down to 25·6% of those in stage 3b; the operation mortality was 3·1%. For the 393 patients treated by radical mastectomy combined with radiotherapy the average five-year survival-rate was 39·9% of traced cases, ranging from 64·1% of those in stage 1 down to 30·1% of those in stage 3b. For 133 patients submitted to local mastectomy alone, the five-year survival-rate ranged from 59·6% of traced cases in stage 1 down to 19·0% in stage 3b; these results were improved when local mastectomy was supplemented by radiotherapy. Actuarially it was found that radical mastectomy gave a five-year expectation of life ranging from 91·03% of normal in stage 1 down to 68·4% of normal in stage 3b; postoperative irradiation improved these results by 4·3% in stage 3b, but for other stages the results were not so good as those of radical mastectomy alone.

1. Harnett, W. L. *Brit. J. Cancer*, 1948, 2, 212.

THE INDEX and title-page to Vol. II, 1948, which was completed with THE LANCET of Dec. 25, is now in preparation. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Digitized by Google

The Wider World

NUTRITION AND HEALTH OF CHILDREN IN FIVE COUNTRIES OF SOUTH AMERICA

R. PASSMORE
M.A., D.M. Oxfd, F.R.S.E.
Of the Department of Public Health and Social Medicine, Edinburgh

5. Colombia

Colombia is a vast region consisting of many large areas with utterly different climates and different economic potentialities, separated from each other by great mountain and river barriers which impede trade, economic development, and the functioning of health services. Thus, like Peru and Bolivia, Colombia flies her flag over an enormous area of the upper reaches of the Amazon river system: here is, for the most part, tropical jungle, thinly populated, chiefly by primitive savages. On the other hand, many of her people live high up on the Andes in a temperate or cold climate, while others have their homes in broad valleys, lying between the mountain ranges, where the climate is semitropical. Some of these valleys are extraordinarily fertile: in one of them which I visited there were large dairy herds grazing in fields where the herbage was as high as the bellies of the cows, and an enormous variety of tropical fruits grew in luxuriant profusion. Both on the Atlantic and Pacific coasts and in the big river valleys, there are large populations dwelling in a humid, tropical climate.

With these different climates agricultural production and food habits vary greatly. The principal foods are maize and mandioca, but large quantities of potatoes, rice, and wheat are grown in some areas. The milk-supply, notably in the large towns, is very inadequate, and supplies of animal fats and proteins are everywhere limited. In parts of the country alcohol consumption is very high. The principal drink is a maize beer, *chicha*, which is home-produced. Young children are sometimes freely fed on this potent beverage, and in some families it provides as much as half the total calorie intake. Animal experiments are now in progress to ascertain its nutritive properties and its effect on growth and development. In Bogota, the capital, burnt-out blocks of buildings will long provide the citizens with visible evidence of some of the social consequences of this drink.

Colombia is for the most part self-supporting in food. Her wealth lies chiefly in agriculture, and before the war coffee accounted for 60% of her export trade.

The population, of just over 10 million, are nearly all of mixed European, Negro, and Indian origin. In the tropical districts there is a free admixture of European and Negro, and in the mountains of European and Indian. This interbreeding appears to have gone so far that there is little or no colour problem.

Colombia differs from most South American countries in one important respect: the intellectual, social, and economic life of the country is not dominated by the capital. Only about 5% of Colombians live in Bogota, and in many ways it has a very precarious hold over some of the provinces. This lack of a strong central government prevents any uniformity in the administration of the health services, but does allow for, and indeed necessitates, provincial enterprise.

HEALTH RECORDS

The following vital statistics are taken from official records.

	Colombia 1945	*Bogota 1947*
Population	10,097,840	492,427
Urban population	30%	..
Birth-rate	31	35·7
Death-rate	16	16·5
Infant mortality	148	146
Stillbirth-rate	53	37
Percentage of total deaths occurring under five years	48	42

These records provide a striking example of South American statistical methods. In the main statistical record for 1945, 40 pages are devoted to an elaborate classification of causes of death in the country, using the international system of nomenclature of diseases. At the end it is mentioned that 70% of deaths in Colombia are not notified by a medical certificate. For what they are worth, the figures suggest a high incidence of deaths from infectious diseases—of which tuberculosis, pneumonia, whooping-cough, typhoid, and gastro-enteritis of childhood appear to be the most important—and this statement is in conformity with all current medical opinion.

The great disease of Colombia is *yellow fever*, which in the past has at times paralysed the whole economic life of the country, and is still capable of repeating its ravages. A reservoir of the virus exists in the jungle districts to the east of the mountains, in the thinly inhabited upper reaches of the Amazon river system. In this region last year 77 deaths from yellow fever were diagnosed by the viscerotome service organised by the Carlos Findlay Institute. The suitable insect vector for the virus flourishes in many of the cities. A single traveller by aeroplane could bring the virus from the jungle reservoir to a thickly populated urban district and initiate an epidemic. A widespread system of immunisation is available and has already protected large numbers of the population.

The high death-rate in early childhood is a measure of the poor health of the children in the country. In Bogota I saw much evidence of primary poverty, and many of the children are undoubtedly not getting enough to eat. I saw isolated cases of rickets, infantile pellagra, and nutritional œdema, but no evidence of deficiency diseases on a large scale.

THE NUTRITION INSTITUTE

Colombia has the best nutrition department of any country which I visited. The whole-time director, Dr. Horatio Parra, is a man of wide experience, and under him are two doctors and four chemists with technical assistance. The institute is now running two children's clinics in Bogota, which should provide valuable data. It has a well-equipped laboratory, and in the last two years a very complete analysis of the nutritive value of Colombian foods has been carried out.

The field work of the department has so far been concentrated on *goitre*, which is endemic in many districts in Colombia. A recent survey of 140,013 school-children in ten departments showed a goitre incidence of 56·5%. This was correlated with a low iodine content of the drinking-water. In the districts where goitre is common, it affects adversely both physical and intellectual development. The problem is to be tackled by wholesale iodisation of table salt, and the institute has been made responsible for the chemical control of this.

The institute will now be able to organise dietary field studies. In Colombia, as in all other countries visited, I was continually told about the ignorance of the mothers as to what constitutes a proper diet for their children. This is an idea freely exported from many public-health courses in the United States. I heard of no attempts to find out the extent and details of this alleged ignorance; yet such details should be basic to any campaign for health education. My guess would be that mothers in South America, and elsewhere, have a fair instinctive knowledge of what foods are good for them and their children, and that poverty does far more than maternal ignorance in determining the bad feeding of children.

Digitized by Google

SCHOOL MEALS

In Bogotá the catering for school meals has been let out to contractors, and I was able to see a copy of the contract. This was a remarkable document. Detailed day-to-day menus were laid down, but for very few items were the quantities specified. Thus on certain days the children were to get a cup of cocoa with milk, a plate of rice with meat and vegetables, and so on. The Nutrition Institute, analysing samples of the ensuing meals, has found that sometimes as much as 80% of the calories was provided by carbohydrate.

The city of Medellin, with 30,000 school-children, is a great contrast in this respect to the capital. Here 2000 midday meals are provided free for necessitous children. The food is prepared in a single centre and sent out to schools. I saw one meal; it consisted of 500 ml. of milk (pasteurised and clearly with a high fat content), a large whole-wheat sandwich with a slice of meat, a slice of tomato and a little cabbage, an orange, and a lump of unrefined sugar.

In the whole country 55,000 children are reported to receive school meals. Neither the diet scales nor the administration are standardised. Medellin and Bogota are probably examples of the extremes of effectiveness of the schemes.

CHILDREN'S ORGANISATIONS

In 1945 Colombia had 58 Gotas de Leche (infant centres), 30 day nurseries, 5 milk centres, 85 clinics for healthy children, 120 clinics for sick children, 15 children's hospitals, and 7 children's gardens. Nearly 90,000 children attended these institutions and over 3 million bottles of milk were distributed.

Most of the milk is distributed by the Gotas de Leche, and the one I saw in operation was issuing a milk-sugar-flour mixture for infants one to two years old. The preparation and distribution of the bottles was in the hands of conscientious Catholic sisters. The composition of the mixture varied from day to day, but usually each bottle contained 200 ml. The Gotas de Leche are a private organisation, but receive some financial support from the government.

At these institutions, in 1945, 38,000 children were immunised against smallpox and 10,000 against diphtheria and other bacterial disease. Neither the immunisation nor the feeding services can in any way cover the needs of the children: the majority never come within their scope.

My last morning's observations in South America illustrate the difficulties in judging children's services.

I was first taken by the municipal public-health staff of a provincial capital to visit the children's hospital. This is a separate building in the main hospital group, with accommodation for 130 beds. The building is modern and structurally good. There is an isolation ward with about 20 beds. In this ward, in which there were no separate cubicles, there were patients reputed to be suffering from chickenpox, meningitis, Vincent's angina, typhoid, typhus, whooping-cough, measles, and gastro-enteritis. There appears to be no bacteriological or serological diagnostic service, so accurate diagnosis was impossible, but I certainly heard whoops and saw a measles rash and some pocks. Those children that were not confined to bed were playing around together. The whole ward was a complete medical muddle—if not a public scandal.

Then I was put in a car and driven 10 miles to a holiday home for schoolgirls, which takes 100 girls for three months on medical recommendation. The home is in a well-built two-storied house round a central courtyard. It is in a beautiful countryside and has a large garden with prolific vegetable crops. There is a fine swimming-bath, a good kitchen, a laundry, and a sick-bay. The house was spotlessly clean and the two women in charge were clearly competent and enthusiastic. The girls looked well and happy. Any municipality in the world would be glad to own this beautiful home and could admire its administration.

It is contrasts like these—so frequent in all the countries visited—that make generalisation about children's health services so impossible.

Special Articles

WHITHER MEDICINE?

THIS was the title of an address by LORD HORDER to the West London Medico-Chirurgical Society on Feb. 18. A man from Mars, he said, would think the question unintelligent. Whither, indeed, except straight on, forging more weapons, taking more toll of science in the interests of mankind, adding more and more culture to more and more learning. He would point out that medicine had already dealt, not unsuccessfully, with the simpler and grosser causes of bodily disablement, that men no longer died in swathes as a result of plague, smallpox, or typhoid fever, and that life had been lengthened. But he would also discover many victims of what was called high blood-pressure and cardio-vascular degeneration; he would find no lessening of psychoneuroses, and, as for the spirit of man rather than the body, he would say that we had not yet begun to develop that.

Today there had been opened for the statesman, the sociologist, and the doctor a large field for inquiry and action. The medical man could not neglect that field; he must take his part in it, though he must not spend in it the whole of his time. He must get apart like Harvey, when he walked up and down under the trees of Combe, thinking. He must not get absorbed and lost in what the statesman and the sociologist happened to be thinking at the moment. They were opportunists; medicine was permanent. To stand aloof from the work that was going on in this field was to do a disservice not only to society but to medicine itself, and yet to become entirely absorbed in it was to do an even greater disservice.

Supposing medicine was given the chance of helping the State by making constructive suggestions, what would those suggestions be? Granted that certain basic desiderata were forthcoming—namely, that medical services were equipped to provide everything that science could offer for the preservation of health and the cure of disease—these must be made available to the entire population. The public should be encouraged to take a vital interest in the plans for its health and happiness and be represented in the formulation of such plans: but inasmuch as it was the doctor who must render these medical services, he should play the dominant rôle. Quality in medical service must be preserved. Adequate hospital facilities, with professional and non-professional personnel, must be available before the scheme came into operation, instead of trusting to a lucky hazard that all these would arrive later on. Finally, Government help, preferably by grants-in-aid, would be necessary. Some method of grants-in-aid seemed to offer the greatest promise because only by that method could the citizen be kept "on his toes" in respect of his own health. But medicine would have failed in an important part of its duty if it did not warn the State that if the more basic needs of the citizen were not met, the direct contribution of medicine would avail little. By "basic needs" he meant proper food, suitable shelter, a satisfactory job of work, fresh air and sun, and reasonable leisure for the enjoyment of the amenities of life. And that was the State's job.

In his closing passages Lord Horder touched allusively upon recent events. It almost seemed, he said, as though doctors were becoming politicians by force majeure. Osler, he thought, would have resisted any allurement of politics: he would have ordered his sailors to bind him to the mast until the danger was over. An attitude of calm detachment would have characterised him. It was paramount that medicine should remain detached from political clamour on the Left or the Right. For medicine there could be no Left or Right, only the seeking of expert knowledge and adherence to the truth.

> "If," said Lord Horder, "I have seemed sententious I crave forgiveness, but here is something to be sententious about. I have spent a long life in the service of medicine. If I have one regret it is a personal one, that I have fallen very short of my own ideals. But my allegiance to medicine is a sort of conditioned reflex. I can do no other, so help me, God! And I will continue to serve medicine, shoulder to shoulder with those colleagues who have seen the same vision and followed the same gleam."

Digitized by Google

Disabilities

25. STAMMERING

THERE may be purely physical stammers, but the speech impediment which tormented my youth did not belong to that category; it was largely a psychological disturbance. Whatever the initial reason for the disturbance which manifested itself in that way, a train of consequences was produced which, looking back, seems inevitable. The proof of my stammering's psychological nature is simple. Never, even during my worst periods, was I unable to speak fluently alone. And if, when reading aloud to myself alone, I imagined I had an audience, or the telephone bell rang, I would immediately start to falter because the fear had leapt into my consciousness again. I know now, of course, that my speech difficulties were inextricably mingled with the more normal trials and tribulations which affect sensitive and difficult natures in childhood and adolescence.

A few days after my ninth birthday I remember walking along a country road, on my way to a party, and hoping that nobody would ask me my age because I doubted my ability to say nine. I have no knowledge of the cause of that anxiety, but this is my earliest recollection of stammering. It seems that the various complex causes which produce shyness in many children in my case produced shyness plus a speech defect. It is not difficult to imagine that this combination must lead to a vicious circle.

Shortly after I arrived at my boarding-school, at the age of ten, Matron asked me what I wanted to be. When I said I might go into the Army she said they would never take me unless I controlled my stammer. This aspect of my speech impediment had not occurred to me before; it was later to assume a dominant place in my thoughts. Two years later, my desires having in the meantime switched to the Navy, I went before an Admiralty board for interview, fully conscious that my stammer would have a critical effect on the result. At the interview an Admiral brusquely asked me if it was getting any better. When I answered "I think so," for in truth I did not know, he replied "You ought not to think, you ought to *know*." I did know from that moment that I had failed. The possibility of failing for any other reason had not worried me at all, and the disappointment I suffered was more due to pride than anything else, for the matron had been proved right.

My next recollection is standing up in class during a French lesson and being unable to get out my answer. "Confound you boy," said the master, "I believe you do it on purpose to avoid doing your homework." The uncomprehending unfairness of this remark made a deep impression on me. It was evident that grown-ups did not understand that it was more important to speak freely than to learn a lesson—a rational conclusion considering that nobody had ever discussed my impediment with me in such a way as to draw me out into truthfulness.

Looking back now it seems that at the age of thirteen, or thereabouts, I had already deeply engraved on my mental make-up the three fears which poisoned my life for many years: the fear of having to speak because I might not be able to do so; the fear of not being able to make my way in life because I could not speak properly; and the fear that I might be thought to be stammering on purpose as a cunning method of shirking. Those fears have been overcome gradually by the exercise of adult reasoning, and by proving by experience that I can compete with the world on even terms. But what troubles would have been saved had I learnt earlier the meaning of President Roosevelt's famous dictum—"There is nothing to fear but fear itself."

At school I was by no means unhappy, and took part in all the usual activities of work and play. I was never "ragged" by the other boys, and I had no difficulty in keeping well to the fore among those of my own age; in due course I held almost every appointment that a school can offer, including head of the school, senior N.C.O. of the O.T.C., and games captaincies. But though it might appear superficially that the disability was no great handicap to results, the nervous wear and tear was tremendous. The policy of the school appeared to be that my speech defect was not to excuse me from any duties, provided I did not object to carrying them out, and pride made that impossible. Nobody can have known what agonies of anticipation some of those duties caused, because pride also never allowed me to divulge them. I remember lying awake in the holidays before I was made a prefect, sweating with anxiety, with my heart palpitating, only to be quietened by a great effort of the imagination whereby I saw myself, proud and happy, reading the lesson fluently before a large congregation in the school chapel.

For many years such mental tortures had to be faced every day, and they ranged from the trivial, such as asking a simple question, to the agony of more public performances. Fortunately, in the active competitive life of a schoolboy it was impossible to dwell overlong over any particular incident, and the bitterness of speech failures was compensated by other successes. The only direct practical assistance I received during my school days was from a housemaster who initiated breathing lessons, and my gratitude for this was tempered with youthful resentment, because the exercises made me spend more time thinking about something which I intensely desired to forget.

The fear of speech often became concentrated on certain consonants—sometimes one, sometimes another. I used to wonder why if I was worried about one consonant I temporarily ceased to be embarrassed by another which had caused difficulty before. It seemed as if my capacity for fear was limited. I grew cunning in avoiding the consonants and words I feared, and adept at quickly substituting others, so quickly that I had no time to be afraid of them. I have even known myself, when shopping, buy some trinket I did not want when unable to say what I did want; a situation which may seem comical to others (I have seen it used in a comic paper) but is fraught with humiliation for the sufferer.

The constant mental stresses associated with speech inevitably caused much introspection. They also drove me into solitude for relaxation, when the routine of life made that possible, as it was during the holidays. I developed an intense dislike of social activities, not for themselves but for the torments they caused. A feeling of frustration was associated with this, because at heart I wished to be like everybody else and enjoy myself in company.

At the university, free from the external pressures of tradition and public opinion which drive on the individual at a boarding-school, my disability dictated my actions more than before. As a result, though I did well at book studies, working probably too conscientiously for the wrong reasons, the speech fears took a greater hold than before, and all the time I was haunted by the thought, appalling to youthful pride yearning to be independent, that few careers were possible to me. Fortunately, however, I had developed a real interest in a branch of study with good openings overseas under circumstances where my handicap would be minimised, and in due course I found myself in a job. Working overseas the pattern of my fears went on much the same as before, though a greater contact with the world produced a more balanced outlook. Only one new terror entered my life—the telephone, which could produce in

Digitized by Google

me all the symptoms of acute fear, so that I loathed the instrument.

In my early thirties I had several periods of profound mental depression on returning to civilisation after months of more simple life in an undeveloped country. It became apparent to me that the dominant reason for these depressions was the contrast between the two sorts of life, one with few speech worries, the other so full of them that it caused all the old fears to return. I visited psychologists and other experts, but they added to my conviction that help could only come from myself. So I gave up my "safe" job, got married, took another job in more civilised surroundings, and stopped what I saw was a partial running away from the difficulties of environment; partial because I had a genuine interest in my pioneer work for its own sake. From that time progress has been wholly in the right direction. This has been greatly assisted by the responsibilities of marriage, which inevitably reduce introspection and turn one's mind to helping others. The war also helped, because this time when I volunteered I was accepted, had the good fortune of getting a direct commission, and ultimately attained a respectable rank in charge of a staff unit, thus showing that Matron had been wrong after all. The vicious circle was now completely broken and I could face life directly, almost free from speech inhibitions and their consequences. If I falter still at times that is now of no great importance and will correct itself in due course. It had taken me over thirty years to accumulate sufficient experience to overcome the original psychological disturbance.

* * *

I can imagine no disability so likely to lead to introspection and self-consciousness as stammering. To be dumb would be a greater affliction but probably not a perpetual worry; that sort of major disability creates a practical problem which has only one answer, and a certain amount of satisfaction is doubtless to be obtained from its solution. I did not know the answer to my stammer, for when the problem was first presented to me I was not old enough to know what it was all about, and the solution should have been found before the vicious circle had time to develop. To attempt to cure a stammer many years after the start by doing breathing exercises is like trying to cure a cold by blowing the nose; some temporary relief may be obtained, but nothing permanent.

I conclude therefore that it is necessary to make a ruthless study of the environment of any child who is beginning to stammer, because it is almost certain that therein lies the root of the trouble. If causes of the emotional disturbance can be discovered and removed, while at the same time remedial exercises are carried out, there should be a good chance of success; but a laissez faire policy will probably condemn the sufferer to a long hard struggle. Which is ultimately best for him is a question on which one cannot generalise, because the answer depends on one's sense of values. I suspect that I have achieved rather more in some directions through having a stammer than I would have achieved without it; but it was certainly at the cost of much unhappiness.

". . . If comprehensive medicine means medicine more closely related to the patient—his life history, his present environment, and his overall needs—it will hardly be possible to teach it to the oncoming generation of medical students without many changes in schools and hospitals. New subject matter, new teaching methods, new clinical experiences will be needed. The factor most conspicuously lacking in medical education—integration—must somehow be provided."—Report of the Commonwealth Fund for the year ending Sept. 30, 1948.

In England Now

A Running Commentary by Peripatetic Correspondents

My walkie-talkie outfit is a great success and I would not now like to be without it. It was installed for me six months ago, since when it has required no expert attention at all. The equipment consists of a big fixed set, driven off the electric mains, and a small portable one worked by the car battery. The big one is a very high frequency transmitter and receiver, the size of a large table wireless-set, which we keep in the hall at home, connected to an aerial on the roof. In the car there is the small set in the boot and a police aerial on the roof, with a small loudspeaker and control panel combined under the dashboard (this does not show unless one looks for it), and a hand microphone. I have two wavelengths. My house transmits on 79·425 mc./s. (megacycles per second, I believe) and the car transmits on 72·925 mc./s. I have an experimental licence granted by the G.P.O. for £15 a year—a bit steep, I think, seeing that I am supposed to be performing a service to humanity.

The technique we have adopted is this. If the people at my home want to get in touch with me when I am out visiting they switch on their set but do no more until I give them a call, which I do pretty often. I do not keep the car set going all the time, because I am in my car only for a very short time between each visit and it would be an unnecessary strain on my car battery. When my car set has warmed up (½–1 min.) I give my call-sign (the name of our house)—"Calling So-and-so. Calling So-and-so. Over"—and wait for a reply. If they have a message for me and the home set is on, my voice goes booming through the house over the loudspeaker and they come and answer me: "So-and-so calling. So-and-so calling. I have a message for you." and they read it out. When they have finished they say "over" and I tell them that I have their message or ask for more information and so on. If they have no message for me they simply do not switch on and I get no reply when I call them. Both of us cannot talk at the same time, because we have different wave-lengths.

The radio-telephone has been an enormous help to me, for I can now get my messages as they come into the house; and it has been an even greater help to my household, who no longer have to chase round after me on the telephone. Within a week of having it installed I left the nursing-home after a fairly normal confinement to see a couple of patients five miles away and should have been off the map for an hour. I called my house when I was going along, and got a message that I was wanted very urgently back at the nursing-home. My patient had had a fairly large pulmonary embolus and was desperately ill for a day or two. I am sure that it was only prompt measures that saved her life. We all blessed the walkie-talkie that day.

It has a radius of action much greater than I need. My house is fortunately on high ground and reception is loud and clear for several miles, except when the car is in a steep dip when the reception fades quite dramatically. This does not matter, of course, as one just avoids using the set on very low ground.

If and when they have health centres the radio-telephone would be invaluable, for the centre could have a fixed transmitter and all the local docs a portable set in their cars. The only snag I see in its general use by G.P.s is its cost. The house transmitter is now £160 and the car set £135. The charge for installing the whole thing was £5 5*s*. Incidentally, we oughtn't really to call it a walkie-talkie, because that is a much lighter affair, with too short a range for my purpose.

* * *

My fellow-peripatetic may like to know that his experience of diabetes tallies absolutely with our own.

When we first started in general practice, the education of our diabetic patients was tackled with all the enthusiasm and love of academic detail shown by Lawrence himself. We circulated copies of his book among the patients, urged them to buy adequate scales, familiarised them with the principles on which Line Rationing is based, and got them word-perfect on the

Digitized by Google

properties of the various preparations of insulin. The more intelligent were even taught to test their own urine for sugar and to appreciate significant deviations from their particular norm.

Most of them came to the conclusion that diabetes was a whole-time job and seemed rather inclined to reorder their lives accordingly. But we were very successful in curing them of any anxiety about diabetes itself; in their fear of offending against any of the rules laid down for its proper management, they lost sight of the disease and had very little time in which to worry about themselves. This seemed a good thing in itself, but we began to wonder after a bit whether it was not perhaps too dearly bought.

Subsequent experience showed that it was; our ineducable diabetics—who forgot, or couldn't be bothered, or didn't understand—flourished just as much as the obsessionally law-abiding variety, without enduring any of the hardships imposed on the latter. They taught us a very valuable lesson, while keeping up a chorus of apologies for failing to carry out this, that, and the other order.

The lesson is that the most important thing about any ailment is the patient's attitude towards it, and the extent to which the ailment is allowed to interfere with the patient's normal life and activities. A diabetic who lives for his diabetes, however correctly and successfully, leads a worthless life compared with the patient who ignores it and goes about his business unconcernedly.

It is the duty of the general practitioner to cultivate this unconcern, having previously reached his own conclusion about the extent to which the disease may be allowed to dominate the patient in any given case. Obviously, this will vary enormously according to the patient's age, temperament, occupation, and a host of other details, all of which the general practitioner will take into account and weigh up very carefully.

It is perhaps this function more than any other which constitutes the specialty of the general practitioner; certainly no-one within the profession attempts to compete with him, or lays claims to the experience which is needed to guide a patient through a maze of difficulties to the right decision about himself.

Mr. Layton in his letter last week puts the case for the general practitioner quite admirably; of all the forces which intimately affect the course of people's lives, the general practitioner is perhaps the most unspectacular and dignified figure, and a Royal College would best fit his stature. He has never shown any marked tendency to embellish his name with academic distinctions, but the profession surely owes itself something here? It is willing and able to acknowledge the services of the man who has performed 20,000 careful tonsillectomies by giving him specialist status and the F.R.C.S.; it lacks a sense of proportion if it has no means of distinguishing the man who has made an equal number of careful decisions about the management of the lives of ordinary men and women.

* * *

What is the doctor? I can answer that:
One who produces rabbits from a hat.
A sort of conjuror; the trouble is
Neither the rabbits nor the hat are his.
He conjures remedies by day and night
Till Nature deigns to put the matter right.
A generation seeking for a sign
Confronts the doctor with the dotted line,
Gives him a pen for wand—and sign he must
And go on signing till he die; or bust.

* * *

My opposite-number grandfather was cited for a knighthood in the New Year's Honours. His two grandchildren—æt. 9 and 7—were not told of the honour lest they should talk, and perhaps swank; but they went to a party where various adults said, "Aren't you pleased about your Grandad?" &c. Their mother called for them after the party and the small boy aged 9 said, "Mum, what is all this about Grandad?" So she replied, "Well, little man, the King is so pleased about the work Grandad has done at the university that he has made him a knight." "Oh Mummy, how awful, how terrible; Grandad will have to go and fight." Voice from the 7-year-old: "Don't be silly, Robin, you know Grandad has no hard clothes."

Letters to the Editor

ACADEMIC FREEDOM AND THE HEALTH ACT

SIR,—Mr. Reginald Payne's letter in your last issue may do harm at a time when medical politics need more light and less heat. He is vulnerable at many points, but I propose to deal with only one—his fear of "the State." He speaks of "the State monopoly" of institutions of clinical instruction, of "dependence on the State," and of "State coercion." Teachers of medicine, he says, have become "State servants" and "Government clinicians," which he finds deplorable. He regards the State as particularly sinister in two spheres, its control over medical education and its influence upon the Central Health Services Council and the other central committees set up by the Minister under the National Health Service Act.

If to be paid by the State makes a teacher of medicine a State servant, the first "Government clinicians" were presumably those very medical professors for whom Mr. Payne feels such concern—the directors and assistants of the professorial units which were set up by the State nearly 30 years ago and receive their pay from the Treasury through the University Grants Committee. I have known many members of the staffs of these units. I am not sure how they would have manifested subservience to the State, but I have always admired their independence of outlook and their loyalty to the highest traditions of the university to which they felt they owed their allegiance, and in these qualities I do not think that they have differed from the non-medical teachers of universities which have been so generously subsidised by the State through the same channels.

Moreover these professorial units were set up by the Medical Research Council—another State body which, though in Mr. Payne's view handicapped by being composed of civil servants and "Government nominees," has to its credit a generation of devoted service to research. Is there any reason why all teachers of medicine today, recognised and paid by the universities for their teaching work, should show any more subservience to the State than the members of the professorial units have done in the past?

What of the "packed" Central Health Services Council and its committees? Are they really in a position of "political tutelage"? It has long been the practice in this country for Ministers from time to time to call into informal conference individuals and members of bodies interested in projected legislation or current problems. Those who have thus advised the Minister have never felt that they have sacrificed their independence by doing so, nor has their freedom of speech been in any way restricted. The Central Health Services Council and its committees embody this valuable procedure in statutory form, and it is surely wise to see how they work before condemning them.

After all, what is "the State"—that emotive abstraction—in the present connexion? It is the medical officers and lay officials of the Ministry of Health. Is it better that they should be left to run the service without outside help, or that they should be able to turn for counsel and criticism to committees, which also have the power to raise matters with the Minister himself? What is the source of the coercion which is to silence these bodies or intimidate them into acquiescence? It exists only in an imagination which can see, behind an iron curtain in some basement in the Ministry, the pitiless lights already being tested, and the ordeal of protracted insomnia in store for the presidents of the Royal Colleges.

London, W.1. W. RUSSELL BRAIN.

FELLOWSHIP FOR FREEDOM IN MEDICINE

SIR,—Your report on Feb. 26 of the recent meeting of this body, at which the restoration of practice goodwill was made a plank in their platform, is disturbing. Such restoration may eventually prove desirable, but a trial really ought to be made with the present system. If the Fellowship propose that the doctor is to rely a good deal in his retirement on the income he gets by investing the value of his practice, they must consider how small

Digitized by Google

it will be. Saving is very hard; as provision for superannuation the Government's present scheme has proved good enough to prevent all but a few from opting out. The alternative method, of investing in Government securities or industrial shares, is unremunerative or risky, with international trade hampered by destruction and national prejudice. If doctors want to retire on a decent income, they have more hope of influencing the Government than the stock market.

It would be unstatesmanlike to introduce a demand for the restoration of ownership into general negotiations now. To grant the demand would have great practical difficulties and would only prolong present uncertainty. And, for the reasons in my first paragraph, the profession would still be left insufficiently protected. Having got ownership we might quite well be compelled to ask for superannuation as well; but the public is not likely to support a demand for the right to buy and sell State pensions.

The president of the Fellowship is a great physician. What he says on clinical matters goes home with all of us. But by lending his influence to reopen a fight at this moment, on the very point on which this Government is bound to be most obdurate, he could do inadvisable damage to relations between the Government and the profession. As a consultant I have in mind particularly the joint committee for advising the Minister on the remuneration of consultants and specialists. There is reason to think it has built up an amicable atmosphere within itself and with the Ministry. In the past I have criticised the B.M.A. strongly, but I would like to pay tribute to its members on that committee: I have confidence in them. They in their turn have paid tribute to the college representatives, who have evidently proved, as I felt sure, understanding and helpful. Good will has done much and I believe will do more. To start a new battle would be deplorable, and for that reason the resolution of the Fellowship, which means as much, is disturbing.

Hove. W. A. BOURNE.

PRACTICE OUTSIDE THE SERVICE

SIR,—Your peripatetic correspondent's account last week of his practice outside "the scheme" must have offered encouragement to all of us who chose as he did. One point I would like to make. He says he formerly served a wide range of "income levels," but now finds himself the doctor of a class "distinct from wage-earners and the poor."

Here my experience does not coincide with his. Since sadly saying farewell to my panel of 1300 on July 5, I have continued my surgeries as before, charging 5*s.* or 3*s.* 6*d.* or occasionally 2*s.* 6*d.* to my former insured patients and to anyone else of the same income-level. This is proving popular, and not alone to my former patients. I still attend, in consequence, a number of wage-earners. The only people I am debarred from treating are the poor and the old-age pensioners. Though I am willing to treat them free of charge as I used to do, they are quite unable to pay the chemist's bill. Perforce they must use "the National." The pensioners will die off in the next 10-15 years, but in the meantime this compulsion bears hard on them, and many resent it bitterly.

London, S.W.10. A. E. BERYL HARDING.

THE OPTICIAN'S TRAINING

SIR,—With reference to Mr. Shaw's letter in your issue of Feb. 26, I must refute the absurd idea that an ophthalmic optician can qualify in six months or by a correspondence course.

For the last eighteen years my association has insisted upon a period of 3 years' full-time training, including 1 year obtaining clinical experience or the equivalent part-time of approximately 5 years. In addition the general education of an optical student must be of matriculation standard before he can be accepted for an optical course of study at an approved college. For the honours diploma, at least a further year of study must follow after qualification before admission to the honours examination. Some of our members have proceeded beyond this to an M.SC. degree, which means yet another period involving three years' research.

From October next the above periods of training are to be increased. To qualify as an ophthalmic optician in the National Health Service, after acquiring school certificate with requisite credits, will mean 4 years' full-time study, including 1 year's clinical experience or its equivalent part-time. The higher diploma will take an additional 2 years.

After registration, an optician who wishes to work in a hospital under the National Health Service will be required, in addition to the above, to obtain two years' experience as an ophthalmic optician before he is entitled to his commencing salary of £500 a year.

British Optical Association, 65, Brook Street, London, W.1. G. H. GILES Director of Examinations.

NATIONAL FORMULARY

SIR,—The publication of the *National Formulary* [1] should materially assist the coöperation between hospitals and general practitioners which everyone desires, and it is hoped that hospitals will adopt it instead of their private formularies. It is realised, however, that the staffs of teaching hospitals may have some misgivings about placing it without comment in the hands of medical students, since it contains preparations which can justifiably be criticised. We, who are members of the committee and are especially interested in the teaching of medicine, feel that it is desirable to explain why a compilation on which much time has been spent by so many well-informed individuals falls short of the ideal.

The purpose of the *National Formulary* is primarily to ensure that the intentions of the prescriber are effectively carried out. The formulary reflects a picture of the present state of practical therapeutics, and every preparation included in the list is there because it has been demanded or approved by some representative body which has been consulted. The committee has felt obliged to insert many items of which some of its members disapprove, but the formulary does contain practically all the effective drugs, apart from anæsthetics, used in modern medical practice. We should like to anticipate some of the more obvious criticisms.

Though the number of mixtures has been kept low, there are still many which have almost identical actions. Thus there seems little justification for the inclusion of both alkaline and acid mixtures containing on the one hand gentian, and on the other nux vomica, since the dose of $^1/_{90}$ grain of strychnine present in the latter can act only as a simple bitter. The preparation mist. strych. et ferr., on the other hand, which contains $^1/_{36}$ grain of strychnine hydrochloride, also contains iron as ferric chloride, and this is not a satisfactory method of prescribing iron. This group, which is commonly prescribed as "tonics," is difficult to assess scientifically. Its members are given in many instances as placebos. Polypharmacy has been avoided as much as possible, in accordance with the modern tendency to include only a few active drugs in a single preparation. Some exceptions, however, remain, such as mist. gelsem. et hyoscy. co. and caps. vitaminor.; and it has been necessary to retain some time-honoured preparations, the use of which can be criticised. Guy's pill, for example, though an efficient preparation, does not enable the prescriber to vary the dose of digitalis and mercury separately. Greater flexibility is achieved if digitalis and inj. mersalyl. are used independently.

It is difficult to find pharmacological justification for a few preparations, as, for example, inj. strych. hydrochlor. (except in barbiturate poisoning and here other drugs are preferable), lot. plumb. evap., lin. aconit. bellad. et chlorof., tab. papaveret., and elix. caffein. iod.

In the children's section, attention has been paid to palatability, but some preparations betray excessive caution in dosage. Linct. scill. opiat. pro infant., for example, contains 1/444 grain of morphine per dose, and it is doubtful if the grain and a half of chalk which is the sole active ingredient of mist. cret. pro infant. can have much effect.

The percentage composition of many preparations is given in the formulary. Some preparations, such as crem. zinc. et ichtham., are made up from a prescription written in the Imperial system, while others, such as crem. zinc., are compounded on a percentage basis. When converted from one

1. See *Lancet*, Feb. 12, p. 269.

Digitized by Google

system to another this has led to fractional percentages in the first instance, and to odd numbers of grains in the second. It would have been better if a consistent method, and preferably the percentage method, had been used throughout.

It is inevitable, however, that a compilation of this type cannot at the same time seem equally satisfactory to the pharmacist, the pharmacologist, the scientifically minded physician, and the general practitioner. Perhaps it is as good a compromise as could at present be achieved. If the formulary is adopted by all hospitals it will undoubtedly assist in coördinating specialist and general-practitioner treatment, and future editions will benefit by the informed criticism of hospital staffs.

A. E. BARNES P. HAMILL
D. M. DUNLOP D. HUNTER
E. J. WAYNE.

MIRACIL D

SIR,—You were kind enough to publish on Feb. 26 a paper on the treatment of urinary schistosomiasis with 'Miracil D.' There it was shown that after a three-month follow-up a total of 74 cases were cured.

It has now been possible to re-examine on three successive days at six months after treatment 51 of these 74 children. Of the 51, 1 is now passing living eggs, 12 are still passing blackened dead eggs, and the remainder are passing no eggs.

Salisbury, Southern Rhodesia. D. M. BLAIR.

A PICTURE SOUGHT

SIR,—As Sir Adolphe Abrahams observed last week, the illustration about which Dr. Terence East (Feb. 26) inquires occurred as part of an advertisement for Eno's 'Fruit Salt' which was published some time in the 'nineties. The Eno booklet *Sixty Years of Health*, from which I culled this information also shows, as a more modern contrast, an illustration from the *Motor* of March 14, 1911, of the original doctor's successor in the country practice having a wayside consultation with, no doubt, the same hypochondriacal patient whilst they pass one another in their motor-cars. (Is the picture of those spacious days shown in the cartoon true; could the doctor afford to keep a chauffeur, whilst driving himself?) No doubt the next stage will be suitably illustrated in *Flight*, when the consultation will take place in the substratosphere!

Middlesex Hospital, London, W.1. D. N. BARON.

SPLENECTOMY IN KALA-AZAR

SIR,—Although, as Dr. Minchin says in his letter of Feb. 26, it is difficult to see how splenectomy can markedly affect kala-azar, a disease involving the whole reticulo-endothelial system, records suggest that in certain rare cases removal of the spleen has favourably influenced patients who before splenectomy seemed doomed despite intensive chemotherapeutic treatment; and he himself appears to agree that the operation should be considered after proof of drug resistance.

While resistance to treatment in kala-azar may depend upon actual resistance of the parasites themselves to drug, other factors, such as failure of adequate concentration of drug to reach all parasites, or some abnormal metabolism or elimination of drug by the host, may play a part; it is also conceivable that a grossly hypertrophied and abnormal spleen may of itself exert adverse effect.

For example, a young boy with Mediterranean kala-azar recently in the Hospital for Tropical Diseases, London, had a severe and persisting anæmia. Before splenectomy it was impossible to correct this, any improvement resulting from transfusions being rapidly lost; but after the spleen was removed his condition steadily improved without further treatment.

As regards 'Urea stibamine,' it seems doubtful whether this preparation is always as potent as Dr. Minchin suggests. Inconsistency of its action may depend upon variation in its constitution, since it may not be a single substance, and Ghosh, Chopra and Chattergee [1] have reported that the antimony content of different commercial preparations varies from 20 to 43%. Certainly the preparation is not always therapeutically effective. In the case mentioned above, urea stibamine failed, as did repeated courses of 'Neostam,' 'Neostibosan,' 'Pentostam,' stilbamidine, pentamidine, and other compounds. Urea stibamine was the first antimonial drug given to this patient, so its failure could not be attributed to antimony resistance induced by other antimonial drugs used in his treatment.

London, W.1. F. MURGATROYD.

1. *Ind. J. med. Res.* 1928, 16, 461.

HOSPITAL BIOCHEMISTS

SIR,—In the correspondence under this heading some flattering remarks have been made about the capabilities of fellows of the Institute of Medical Laboratory Technology as compared with medical and chemical graduates. The comparison is unfair but prompts me to comment as follows.

There is a growing tendency to accept the capabilities of the fellow of the I.M.L.T. without at the same time offering a salary commensurate with his knowledge and comparable to that paid to similar workers in other spheres. At the present time, senior technicians of 10–20 years' experience are seeing administrative posts in the National Health Service being filled by clerks and others at commencing salaries of £200–400 per annum more than the maximum available to themselves. Already numbers of young technicians are leaving laboratory work, before qualifying, for more lucrative occupations; so not only is there bound to be a decline in the numbers of qualified technicians, but the standard of new entrants is also going to be lowered. In order to retain the services of some of these younger workers, salaries are being offered and paid to them which are far in excess of their worth—which merely aggravates the the position by causing first of all a sense of unfairness in the minds of the senior technicians, and secondly a feeling of frustration in the younger technician, when, having obtained his qualification, he finds himself unable to increase his salary.

The Institute of Medical Laboratory Technology seems unable to do anything in this matter since by virtue of its constitution it is precluded from participating in the joint negotiating committee set up to determine salaries and conditions of service of laboratory technicians. It would appear that the trade unions are the only bodies capable of representing the technician at the J.N.C.

In the past a benevolent eye has been kept upon our activities by the Pathological Society of Great Britain and Ireland, and more recently, perhaps, by the Association of Clinical Pathologists. Whilst we were all dealing personally with our own employing authority this was an ideal arrangement, but in the present day of Ministerial control I feel that the medical profession as a whole might well take up the cudgels on our behalf. Our services to that profession have never been spared.

Wakefield. R. A. WARD.

INDEPENDENCE IN RESEARCH

SIR,—Greek medicine flourished in spite of Plato's opposition, as Mr. Clarke notes (Feb. 26), mainly because of the decentralised nature of Greek society and its strong democratic trend, which prevented unlimited power from falling into the hands of any particular individual, however eminent he might be. This helped to preserve that tolerance for variety of opinions which, in Whitehead's [1] view, is essential for the evolution of real knowledge.

The best works of the Hippocratic Corpus [2] are all truly scientific in spirit. They contain a minimum of speculation and are based largely on observation and critical examination—the simple empirical method praised by the author of *Ancient Medicine* and by most writers of the present day. It is a method which has played an important part in the growth of modern science.

Plato,[3] however, denied that real knowledge could be obtained by the empirical method based on observation.

1. Whitehead, A. N. Science and the Modern World. Cambridge, 1946.
2. Jones, W. H. S., Withington, E. T. Hippocrates. Leob Library, 4 vols. 1923–31.
3. Zeller, E. Outline of the History of Greek Philosophy. London, 1931.

Digitized by Google

He believed that it could be achieved only by revelation through the non-material soul-mind: "the greatest goods become ours through inspiration in virtue of a divine gift." This attitude, as Zeller [3] points out, leaves no place for empirical knowledge, and renders scientific experiments useless, inadequate, and futile. Plato was not simply contemptuous; he was actively hostile. He denounced scientific experiments as "a presumptuous prying of a man into the Divine order of nature." Worse still, he attributed the moral and ethical degeneration of his day to the fact that science had undermined the traditional ties that kept society together. In order to correct this state of affairs he proposed to convert the State into a religious community, with a strict watch over the whole mental and moral life of the citizens. Even poetry, music, and art were to be subjected to strict censorship; and family life and marriage were to be supervised by the State. The individual had no rights and everything had to be subordinated to a plan expressing Plato's own convictions on the way to "live rightly." Those who would not accept his word and "persisted in their error" were to be executed. As Zeller says "with this appeal to force against reason, freedom of thought came under the ban of the state and philosophy was transformed into dogmatism."

At a later period science and rational medicine were rapidly eliminated by the early Christian Church, the aims of which were akin to Plato's, and which possessed the power he lacked to impose its views. For centuries Europe was doomed to be the prey of established intolerance; there was no science and no rational medicine. Unfortunately the rulers of man in the past have nearly always shown an exaggerated confidence in restriction and regimentation [4]; and the increasingly Platonic character of modern trends shows that it is still the case.

Manchester. F. S. A. DORAN.

FEMALE CIRCUMCISION IN THE SUDAN

SIR,—On Feb. 18 Mr. Hector McNeil, Minister of State, said in the House of Commons that, although it was difficult to get accurate figures, he was assured that the practice of Pharaonic circumcision had decreased by 75% in the Khartoum area during the last 20 years. It may be taken for granted, therefore, that his assurance was not based on statistical evidence.

It is no doubt the case that some of the better-educated and more intelligent Sudanese are becoming ashamed of the practice, partly because of the indisputable evidence that it is rooted in pagan superstition, but more perhaps because of the growing realisation that so long as they tolerate the infliction of cruelty on their female children, and of degradation and life-long suffering on their women, they will stand condemned in the eyes of civilised people. For this reason enlightened Sudanese are inclined to minimise the extent of the evil, and to make statements about progress which are not borne out by the facts so far as they are known to the doctors, nurses, and midwives. There is a real danger that the too easy acceptance of optimistic statements based on wishful thinking may weaken the hands of those who are trying to persuade the Sudanese to abandon the practice, at the very time when it is most desirable that their hands should be strengthened.

I am prepared to believe that following the publicity which this question has received in the Sudan since 1945, and the representations which have been made in private, a few leading families in Khartoum may have been persuaded to discontinue Pharaonic circumcision; but those who are in close touch with the problem will not be prepared to accept Mr. McNeil's unsubstantiated statement that the practice has been diminished by 75% in the Khartoum area: proof of such a statement could only be obtained by carrying out a medical examination of all the female children now attending school in that area. Even if the statement regarding the Khartoum area were approximately accurate, the number concerned is so small that it would not invalidate my statement that practically 100% of the girls in northern and central Sudan are subjected to circumcision, and the great majority of them to the ghastly form of mutilation known as Pharaonic circumcision.

Mr. McNeil announced that the Sudan government had appointed a woman doctor. Thirty-two years ago, Dr. Crispin, then director of the Sudan Medical Service, urged the government to appoint a woman doctor as inspector of midwives. His hope was that by acting as the guide, philosopher, and friend of the midwives, she would gain their confidence, and through them that of the women, and that through the influence she could exert in this way the Sudanese would gradually be persuaded to abandon Pharaonic circumcision, or at least to substitute for it the less harmful Egyptian operation. Considering the harm that has been done to the women of the Sudan during these 32 years, it is a real tragedy that his far-sighted recommendation was turned down on the grounds of expense.

In conclusion, might I point out that in Paris, on Dec. 10, 1948, the delegates of the governments of the United Kingdom and Egypt, amongst others, signed a Declaration of Human Rights, article 5 of which reads as follows: "No-one shall be submitted to torture, or to cruel, inhuman or degrading treatment or punishment." The governments of the United Kingdom and Egypt, who are jointly responsible for the administration of the Sudan, seem to have appended their signatures to this document a trifle prematurely.

House of Commons. BASIL NEVEN-SPENCE.

CHEWING THE CUD

SIR,—I was interested to read last week's annotation under this heading.

This rumination is by no means always indicative of disease. It can often be seen in association with the act of vomiting during recovery from ether anæsthesia, particularly in children after tonsillectomy. The rapid up-and-down movement of the lower jaw occurs in the intervals between the bouts of antiperistalsis of the stomach and œsophagus, but horizontal movements are not often seen. I should imagine that it is a very primitive reflex, and perhaps an indication that primordial man was a ruminant and vegetarian. I must in future determine whether or not the children who exhibit this phenomenon tend to have a distaste for meat.

Bangor. JOHN ROBERTS.

GASTRIC CARCINOMA

SIR,—Dr. Wilkinson is one of the few men in a position to tell us how far the incidence of carcinoma of the stomach in addisonian anæmia differs from expectation. The problem is of some practical importance; but it has an even greater theoretical interest, and many of us would be grateful if he could submit his records to actuarial analysis. In order to calculate the expected number of carcinomata in his material,[1] we need to know the number of men and women whom he has followed through various age-groups—that is to say, the number observed in their 31st, 32nd, 33rd, 34th year, and so on up to the solitary patient in his 100th year. Only a very rough calculation can be made from the present figures, but that leads me to believe that his reported total cancer incidence is somewhere between 50% and 150% of expectation.

If full analysis is impossible, a simpler but less accurate calculation could be performed if he merely gave us the age and sex distribution of the gastric carcinomata and of the carcinomata at other sites. Presumably not more than 14 of his 70 carcinomata should have been in the stomach, whereas actually there were 28. Was the localisation of these tumours and the histology similar to other series? At present we are left in the air. The liability of patients with addisonian anæmia to develop gastric carcinoma may be twice expectation, but since expectation is only about 1 per 1000 a year in males in the fifties, and about 2 per 1000 a year in the sixties, doubling expectation hardly justifies the discomfort and expense of repeated investigations.

4. Robinson, J. H. The Mind in the Making. Thinkers' Library, 1940.

1. Wilkinson, J. F. *Lancet*, Feb. 12, p. 249 Feb. 19, p. 291, Feb. 26, p. 336.

Digitized by Google

The real position, however, is more complicated and more interesting than this. I suggest that the incidence of gastric cancer is possibly as high as 1–2% in the first few years after diagnosis, but that after 5 years there is little or no increased incidence. (It is difficult to prove this as there is some uncertainty about the incidence of gastric cancer in the older age-groups in the general population. Jennings [2] gives reasons for supposing that the Registrar-General's death returns seriously underestimate the incidence at ages over 70.) It is worth while investigating a group of patients if there is a 1-in-50 or 1-in-100 chance of finding an operable cancer, but not if the risk is much less or the patients are bad subjects for surgery.

Cancer in an atrophic mucosa can be compared with cancer in the margin of an ulcer. A proportion of apparently simple peptic ulcers prove themselves to be cancerous within 5–6 years of onset, but it is doubtful whether simple ulcers watched for 10 years or more become cancerous. It is probably not the atrophic state or the chronic ulcer which is dangerous, but the possibility that a permanent change in intracellular metabolism has preceded the initial atrophy and the initial ulcer. The ordinary type of gastric ulcer is fairly safe, but when one occurs at an unusual site or in a particularly healthy person the chance of its proving malignant must be taken seriously. Can we make the same sort of distinction with the atrophies? The ordinary achlorhydria associated with diabetes, thyrotoxicosis, and the menopause seems to be safe, but can the same be said for an achlorhydria which rapidly develops for no obvious reason in a duodenal-ulcer patient in the fifties or sixties?

London Hospital, E.1. DENYS JENNINGS.

NO ROOM AT THE HOSPITAL

SIR,—Surely one short-term expedient immediately applicable to the present need for accommodation in London is to secure the admission of patients to the hospitals nearest to their own homes. By the present constitution of the Metropolitan regions patients are being brought from very wide areas to the exclusion of Londoners. When the sectors were originally delineated there were hospitals in the extra-Metropolitan areas which relieved the strain at the centre. The consultants are back in London and expect the patients to be brought to them. While other national services are being organised so as to relieve London, the hospital service has followed the reverse process with the inevitable consequence. LONDONER.

A FACULTY OF GENERAL PRACTICE

SIR,—The suggestion of "F.F.G.P." that there should be a diploma for general practitioners, and that of Mr. T. B. Layton of a Royal College of General Practice, both interest me greatly, having recently made the same suggestions myself [3] and had them warmly received in personal letters.

In the 19th century most doctors were general practitioners, and received their training in man's natural environment—in the home, the family circle, the school, the farm, and the workshop. They met their patients on their own ground, and studied them as natural phenomena conditioned by their environment. That still is the task of the family doctor; but we have now reached the position where he is supposed to be fitted for it by studying the isolated human animal in the entirely artificial surroundings of a hospital, by being given a smattering of the ever-increasing number of specialties, and by being launched on his career as a sort of half-baked protégé of the pukka surgeons, physicians, and obstetricians.

It is true that an attempt has now been made to correct this state of affairs by the scheme of trainee assistants; but this only goes a very small way to meet the real need. The family doctor of the future will have to practise the prevention and cure of disease, and study its evolution, in the home, the school, and the workshop, and his training and outlook should be directed to that end.

2. Jennings, D. *Brit. J. Radiol.* 1947, **20**, 522.
3. *Brit. med. J.* 1948, i, 809; Modern Trends in Public Health. London, 1949; p. 132.

This can only be done through some such body as a Royal College of General Practice, whose duties, as Mr. Layton says, would be to decide the functions of the family doctor and how they are to be carried out, to negotiate his terms of service so that he has every opportunity of carrying them out properly, and to coöperate in his training.

In America it is now possible to be a specialist in heart-block. How absurd that such a man, however able, should be regarded as a suitable mentor for a general practitioner.

Ashtead, Surrey. W. EDWARDS.

SIR,—I am interested in your contributor's letter of Feb. 26; for in my *State Medicine or What?* (1943) the following appears:

"A General Practitioner of more than 10 years' service would be allowed to be graded as a specialist in General Practice."

Again in *Your Doctor of the Future* (1944) I suggested that after 5 years' service the doctor should have the choice of three alternatives: (1) to devote himself to the specialised and scientific side; (2) to turn to the administrative or public-health side; or (3) to specialise in general practice and take a diploma in that branch. Each alternative should be equally attractive.

Worthing. HAROLD LEESON.

GUM-SALINE

SIR,—May I support Mr. Gibberd's advocacy, in your issue of Feb. 26, of gum-saline solution for the restoration of blood volume? This substance must have been used on a very large scale in the 1914–18 war and also between the wars, and in common with others I gave it to many patients in both hospital and domiciliary practice without observing the dangerous effects which were becoming attributed to it in its later years.

The treatment of shock and hæmorrhage in those days was undoubtedly inferior to that possible now. Plasma is of great advantage for commencing a transfusion, as it can be run in quickly; and I have always found it difficult to believe that it is desirable to give ice-cold blood rapidly to a shocked patient. When the patient's condition has improved, the transfusion can be continued with blood at a slower rate, or this can be done on a later occasion; and this has the advantage that Rh-testing can be carried out, if it has not been done previously, and Rh-negative blood economised. The risk of plasma jaundice is, however, a formidable one, and I have had at least three cases in the past two years. It is also probable that plasma will become scarce before long, when war-time stocks have been used up.

The reports on the use of dextran are promising, and it is likely that this or some similar substance will replace plasma in the future. But there still seems to be a place at present for the use of gum-saline, if the manufacturers will only supply it.

Middlesbrough. BRYAN WILLIAMS.

*** We understand that gum-saline is obtainable from Messrs. Crookes Laboratories Ltd.—ED. L.

MEDICAL HISTORY OF THE WAR

SIR,—The writing of the official medical history of the 1939–45 war proceeds. The raw materials out of which it must be built are the reports and the like which headquarters of formations and units were required to send back to the War Office during the war years. These proffer in great abundance factual information which must, of course, guide the historian's pen. But these reports were addressed to the War Office and not to posterity; they tell of what was encountered and of what was done, but seldom do they reveal the reasons for action or disclose its results. They give no expression of the thoughts or feelings of those concerned.

This history, when written, must be more than a mere chronicle, it must distil wisdom out of the experience of a generation so that those who follow can, if they so wish, profit. Blood is well shed if it is to be used in such transfusion.

There must be many who served with the R.A.M.C. who can help very materially if they will but unlock the door of memory or hunt out the diaries of those days and

Digitized by Google

tell of what they know. This is more particularly the case in those campaigns that ended in tactical defeat—France, 1939–40, Norway, Greece, and Crete—for there was much burning of papers, and all that remains to be read is that which is deeply engraved upon the minds of those who served and endured. Then there were the relatively undramatic but nevertheless important affairs in Madagascar and Paiforce, and the isolation of those in West Africa, concerning which there is but little on record.

In this building of a comprehensive and significant picture out of a great mass of apparently unrelated little bits and pieces no information is without value—information not only about matters medical but also concerning the formations with which the medical services were associated. I shall indeed be grateful for any help that I can attract.

Usher Institute,
Warrender Park Road, Edinburgh, 9. F. A. E. CREW.

SUBSCRIPTIONS TO THE LANCET

SIR,—On inquiry among clinical students in this university, I find that few of them subscribe to your journal. This is regrettable; for once the habit of reading your peripatetic correspondence is formed it is unlikely ever to be broken. Having found this page enlightening, they will be tempted to try a leading article, and so on.

It would be a good thing if the student rate of subscription available before the war were again introduced.

Sheffield. A UNIVERSITY TEACHER.

*** We are obliged to our correspondent for his interest. He is, however, misinformed in supposing that the lower rate of subscription for students (£1 1s. per annum) has been discontinued. Applications for such subscriptions are accepted on the same condition as any other applications—namely, that our supply of paper allows us to print the copies required. Though the recent relaxation of control of newsprint for newspapers does not affect periodicals, our quota of paper continues to increase gradually, and a limited number of new subscribers can now be supplied.—ED. L.

Parliament

Analgesia in Childbirth

ON March 4 in the House of Commons Mr. PETER THORNEYCROFT moved the second reading of this Bill. A private member's measure, it was, he emphasised, backed by members of all three political parties, while the National Association of Midwives, the National Council of Women, and the National Federation of Women's Institutes were all solidly behind it. The only person who could stop the Bill from passing was the Minister of Health. Mr. Thorneycroft would be surprised if, after having been associated with a great measure of social reform like the National Health Service, Mr. Bevan could end his name to the obstruction of a Bill so popular in the country and so desirable as this one.

While paying a warm tribute to the pioneer work done by men like Dr. Minnitt, who invented the gas-and-air machine, by Dr. Elam of the Wellhouse Hospital at Barnet, by the National Birthday Trust, by the Central Midwives Board, in the long battle to get any degree of analgesia accepted, Mr. Thorneycroft was astounded that in the hundred years since this principle was first discovered so little progress had been made. In the 1946 survey the number of women attended by midwives in their own homes who got any relief was only 7% in England and only 1 woman in 433 in Wales. In Scotland not one solitary woman attended by a midwife in her own home got any relief at all. Taking all the mothers in the country, whether they had their children in hospital or not, less than half got any relief. Another point which had astonished him was the difference between one area and another. The latest figures showed that out of 350,000 women attended by midwives in their own homes, only 43,000 got some relief. Describing the main provisions of the measure,[1] Mr. Thorneycroft said that its modest character was explained by the fact that as a private member's Bill it must not impose additional public expenditure which had not already been approved in principle by Parliament, but it did turn a permissive power into a public duty.

Dr. HADEN GUEST thought that the most important part of the Bill was that which provided that all midwives should be trained in the giving of analgesia. He hoped that the Government would give an encouraging answer to the debate, and that they would be able to set up at an early date a plan for training midwives over a four-year period, because until properly trained midwives were available real progress was not possible.

Colonel M. STODDART-SCOTT pointed out that in the Ministry of Health Supplementary Estimates, there was an unspent item for £23,000 allocated to refresher courses. Colonel Stoddart-Scott suggested that money could be well spent on courses for midwives.

Dr. STEPHEN TAYLOR contended that if the present rate of progress was continued we would within four years have trained all our midwives without this Bill. The progress in training had taken place only since the Minister of Health took office and put pressure on local authorities. The result had been that 3000 extra midwives had been trained every year. Mr. Thorneycroft had failed to tell the House that instead of 43,000 mothers receiving analgesia little more than 1000 mothers received it in 1938. The rate of progress had been 27,000 mothers for 1946–47, and 43,000 mothers for 1947–48. He hoped that the latest figures would show that the numbers had again been doubled. Since the passing of the National Health Service Act the Minister had fully compulsory powers to apply analgesia. What more was wanted? Turning to technical considerations Dr. Taylor pointed out that unfortunately the gas-and-air machine had limitations, and although they wanted to make it available to everyone there would always be a certain proportion of mothers who would not get relief from it. It also did not give adequate anæsthesia for stitching up after the birth.

Dr. S. SEGAL reminded Dr. Taylor that what the supporters of the Bill wanted to do was not to emphasise that these powers already existed, but to issue a clear categorical directive to every local authority that it must be regarded as their bounden duty under the National Health Service Act to administer analgesics whenever they were required. There was a limit to which the actual degree of pain endured by any patient could be translated into figures. He felt that this Bill would make a definite contribution towards encouraging large families in thousands of homes in the country. In his view there was no excuse for the Government not giving their fullest support to the Bill.

Mr. ARTHUR BLENKINSOP, parliamentary secretary to the Ministry of Health believed, particularly through the operation of the health service, that this country was making rapid and encouraging progress. They were not divided on the objects of the Bill, and there was no desire on the part of the Ministry to check in any way the development of this work. The Minister agreed that the first issue was to secure the full and adequate training of those who would do it. As from Jan. 1, 1948, all new midwifery pupils were being trained in analgesia. In the cities of Birmingham, Bristol, Leeds, Leicester, Liverpool, Manchester and Sunderland, from July to December last year, some 4230 cases had analgesia administered under the domiciliary service as against only 4000 during the whole of 1947. In London at the end of 1946 only 50 out of the 148 council's midwives were trained and qualified. By the end of last year 148 out of 155 were trained. Similarly, in London in 1936 the administration of analgesia in the domiciliary service was used in only 5% of the cases. From July to December of last year the figure had risen to 44%. In December of last year alone it had risen to 60%.

Mr. Blenkinsop agreed that there was still more to be done, and they all wished to bring other authorities to the level of the most progressive. The Government were taking all practical steps to that end. From the continuous development of their vigorous drive on this issue they could, he claimed, secure exactly the same ends as those sought by this Bill. He therefore thought that the measure was superfluous. If they isolated particular portions of the National Health Service by providing special statutory provisions for separate

1. See *Lancet*, Feb. 26, p. 356.

Digitized by Google

elements, the conception of a service covering the whole of our health requirements was likely to be wrecked. He did not believe that this was the best way to ensure the best possible service in this direction, or indeed for any other provision within the Health Service. The Government welcomed the debate because they felt that it would give them added strength in their endeavours to ensure the highest possible service throughout the country, but if full support was given to the efforts of the Ministry and the local authorities in pressing forward with the measures which they were already taking, and which were already bringing the type of response they wanted, the full aims of this Bill would be secured without imposing new duties on the local authorities and new penalties on the hospitals.

Lady TWEEDSMUIR said that all supporters of the Bill would be shocked and astonished by the attitude of the Parliamentary Secretary, which implied that the Bill would be killed in committee.

QUESTION TIME

Grants to the Universities

Sir ERNEST GRAHAM-LITTLE asked the Chancellor of the Exchequer if he would now make a statement regarding the grant to universities which he proposed to make in the forthcoming Budget.—Sir STAFFORD CRIPPS replied: I am providing £12,814,500 for recurrent grants to universities. This amount includes provision for the additional expenditure which universities will incur in bringing into operation the revised scales of payment for teachers in the medical and dental schools. The progress of the universities' scheme for physical expansion necessitates an increase in the amount required for non-recurrent grants, and I am providing £4¾ million for this purpose as against £2,600,000 this year.

National Awards Committee

Sir HUGH LUCAS-TOOTH asked the Minister of Health what remuneration he had in mind for the chairman and members of the National Awards Committee set up on the recommendations of the Spens report on the remuneration of consultants and specialists.—Mr. ANEURIN BEVAN replied: The chairman of the committee is being paid a salary of 3000 guineas for the first year, 2500 guineas for the second, and 2000 guineas for the third. Those members of the committee who are retired receive a fee of 7 guineas for each day given to the work of the committee.

Medical Treatment Abroad

Dr. S. SEGAL asked the Secretary to the Treasury whether he would consider the granting of a special sterling allocation to certain tuberculous patients who could be certified as having become acclimatised to residence only at high altitudes.—Mr. GLENVIL HALL replied: I do not think that it would be appropriate to issue a general instruction in the sense suggested. All applications for foreign currency on health grounds are considered by the Medical Advisory Committee, who base their recommendations on the medical evidence submitted in each individual case. If such evidence included a reference to the effect of climatic conditions on the patient, it would no doubt be taken into account along with other factors. Dr. SEGAL: Is the Minister aware that many patients of this particular group have had their resistance to disease lowered after their return to this country and have died of quite minor ailments; and in connexion with this particular group, would he accept the evidence of foreign doctors resident in Switzerland and urge that upon his medical advisory council?—Mr. GLENVIL HALL: The Medical Advisory Committee do take these factors into account. We must leave it to them. They are the experts in these matters.

Mr. P. W. DONNER asked the Chancellor of the Exchequer in how many cases applications from persons suffering from tuberculosis had been refused foreign exchange in order to be treated or cured in Switzerland.—Sir STAFFORD CRIPPS replied: The number of tuberculosis applications refused for all countries is 101 in the 14 months ended Feb. 14 last. The figure for Switzerland is not separately available, but Switzerland probably accounts for 90% of the tuberculosis cases. The corresponding approvals over the same period were 1009.

Colonel M. STODDART SCOTT asked the Chancellor how many applications for foreign currency for the treatment of disease abroad were considered in 1948: and how many of these applications were refused.—Mr. GLENVIL HALL replied: From January to December, 1948, 2907 of which 914 were refused.

Colonel STODDART-SCOTT asked the Chancellor how many medical members there were on the Exchange Control Medical Advisory Committee; how many times this committee met in 1948; and how many were present at each meeting.—Mr. GLENVIL HALL replied: Ten, exclusive of the secretary and the Treasury medical adviser. There are no non-medical members. The full committee met five times, the numbers present being respectively 10, 9, 10, 11, and 10. In addition, each application is submitted to two members of the committee and, if necessary, to the chairman as well. Members meet informally among themselves at frequent intervals for consultation about cases.

In answer to a further question he added that each member of the committee receives an honorarium of £500 per annum in respect of all services. The total cost in 1948 was about £6500.

General Practitioners in the Service

Mr. WILLIAM KEENAN asked the Minister of Health what was the total number of doctors registered with the National Health Service in the first six months from July 5 last; and what were the average salaries earned by doctors concerned in that period.—Mr. BEVAN replied: The total number of general practitioners on the medical list at July 5 was 18,165. Since then 661 other practitioners have been admitted and approximately the same number have left. I have no information as to the average salaries earned by doctors in that period. Mr. KEENAN: Am I justified in concluding that these doctors are now receiving much greater remuneration than before the Act came into force?—Mr. BEVAN: I must see how the average turns out before I am able to reply to that question. Certain payments are, of course, made to doctors outside the National Health Service Act.

Mr. LOUIS TOLLEY: Can the Minister give the percentage figures of doctors already in the scheme compared with the number who are entitled to join it, and is he satisfied that the number of medical practitioners in Britain is sufficient to meet the needs of the extra demands made upon them by the National Health scheme?—Mr. BEVAN: There are more general practitioners taking part in the administration than we estimated for at the beginning. There is, of course, a general over-all shortage. Perhaps there is a shortage of doctors in some places and a surplus in other places. (Cries of "No.") As the surplus doctors redistribute themselves there ought to be adequate doctors for all.

Regional Hospital Board Economies

Sir PATRICK HANNON asked the Minister if, in view of his request for reductions in the estimates for regional hospital boards, 1949–50, he would keep in view the high standard of hospital administration in Birmingham and the various schemes in process for expansion and development, and would consider representations from the regional hospital board on the limits within which economies could be effected.—Mr. BEVAN replied: Yes, Sir.

Colonel STODDART-SCOTT: Is this not a direct attempt to slash our hospital services? (Cries of "Oh.")

Replying to a further question Mr. BEVAN said this was not a flat-rate reduction, but one which took into account the hospital needs of each particular area.

Certificates for Hearing-aids

Mr. A. J. CHAMPION asked the Minister if, within the health service, there was provision made for any form of appeal from the decision of a doctor not to recommend a hearing-aid.—Mr. BEVAN replied: No, Sir; on treatment the specialist's clinical judgment must be final. The patient first goes to a general practitioner. He then has what he never had before: the opportunity to consult a specialist at a hospital and a proper otologist. If the specialist after examination says that a hearing-aid is useless to him, it is hardly conceivable that there should be an appeal against that decision. It is not a judicial matter.

Beds for the Tuberculous

Mr. MARTIN LINDSAY asked the Minister of Health how many tuberculosis beds there were in the United Kingdom; and whether he had been able to make an assessment of the number of patients awaiting admission to sanatoria.—Mr. BEVAN replied: On the latest figures available for

Digitized by Google

England and Wales there are approximately 33,000 tuberculosis beds, and a waiting-list of about 9000. The figures for Scotland are 6554 and 2721 respectively.

Voluntary Work for the Handicapped

Mr. EDWARD EVANS asked the Minister if he was aware that public support of voluntary organisations for the welfare of the blind and other handicapped persons was being adversely affected by his recent pronouncement regarding hospital collections; and if he would make it clear that the State did not defray the cost of this welfare work.—Mr. BEVAN replied: My pronouncement referred solely to hospitals in the National Health Service. The National Assistance Act fully recognises the valuable work of the voluntary bodies referred to and I am glad to take this opportunity of correcting any impression that they are no longer playing an effective part in the provision of welfare services. Mr. EVANS: Will the Minister also make it clear that the social-security services cannot possibly function without the voluntary welfare services, which depend very largely on the good will of the public for voluntary funds? Will he also make it perfectly clear that blind and deaf persons are not necessarily sick persons?—Mr. BEVAN: I have always expressed the view that the voluntary organisations are the only means by which effective assistance can be given to handicapped classes of all kinds and I fully endorse what my hon. friend has said.

Public Health

Influenza

THERE were 251 deaths from influenza in the great towns of England and Wales during the week ended Feb. 26, compared with 159 during the previous week. There was a slight preponderance of deaths in the north-east (Sunderland 12, South Shields 6) and in the north-west. Greater London had 98 deaths, compared with 85 in the previous week.

Expulsion of Vaccine Lymph

A medical officer of the Ministry of Health writes that anti-smallpox vaccine lymph is now put up in capillary tubes. These are not of uniform size, and the special device which used to be sold for expelling the lymph from the tubes is not always readily available and is sometimes ineffective. A simple alternative is to use a baby's feeding-bottle teat, the open end of which is easily occluded by the thumb. The teat can be sterilised by boiling, and the nipple hole is usually about the right size to make an airtight joint with a capillary tube.

Another method, suggested by Dr. O. H. Bowen, is to break off both ends of the lymph tube and then to insert the sterilised needle of a hypodermic syringe, *with the plunger pulled out*, into one of the open ends. If the junction of tube and needle is surrounded with a small sterile pledget of wet cotton-wool to make an airtight joint, the lymph can be expelled without difficulty by pushing down the plunger of the syringe. Obviously care must be taken to sterilise needle and syringe before these are used for other purposes.

Notification of Infectious Diseases

ENGLAND AND WALES

	Week ended Feb.			
	5	12	19	26*
Cerebrospinal fever	32	30	37	46
Diphtheria	116	148	112	119
Dysentery	75	68	104	79
Encephalitis lethargica	..	..	..	3
Food-poisoning	42	17	19	23
Measles, excluding rubella	13,815	18,441	19,504	20,055
Ophthalmia neonatorum	39	41	45	59
Paratyphoid fever	4	5	9	7
Pneumonia, primary or influenzal	1016	1139	1471	1607
Polioencephalitis	1	3	1	4
Poliomyelitis	9	15	19	10
Puerperal pyrexia	86	93	121	111
Scarlet fever	1372	1417	1334	1262
Smallpox	..	..	..	..
Typhoid fever	6	7	3	4
Whooping-cough	3174	3011	3027	3045

* Unrevised figures.

Industry in 1947

During 1947, 203,236 accidents were reported under the Factories Act, 1937—a decrease of 9·2% compared with 1946. Of these accidents, 839 proved fatal—an increase of 1·6% over the previous year. These figures are given in the annual report of the Chief Inspector of Factories [1] which shows that fatal accidents stood at 72% of the 1937 figure, and that non-fatal accidents, although declining 13% on the previous year, were still 5% higher than in 1937. Such comparisons may, of course, mislead, since the numbers employed, the hours of work, and other factors fluctuate from one year to another; and in 1947 many industries were idle during the fuel crisis.

In his report Mr. G. P. Barnett notes that plans for providing good, healthy, and safe conditions were impeded by continuing shortages. The problems in the pottery and cotton industries were, he says, particularly difficult, with old premises to be reconditioned and modernised, and a labour force to be built up largely from relatively untrained people. Nevertheless improvement was evident. Mechanised handling systems and automatic systems of feeding and charging machines were being brought into use in brick-making, in the construction of buildings, in iron-founding, and in electrolytic plating, among other industries. As in previous years,[2] comment is made on the use of unsuitable premises for factories—a practice which became largely controllable under the Factories Act of 1948. There were notable developments in personnel management; by the end of the year some 55% of factories employing over 250 people had at least one full-time personnel officer or welfare supervisor.

1. Annual Report of the Chief Inspector of Factories for the Year 1947. Cmd. 7621. H.M. Stationery Office. Pp. 127. 2s. 6d.
2. See *Lancet*, 1947, i, 30; *Ibid*, 1948, i, 298.

Births, Marriages, and Deaths

BIRTHS

ALLEN.—On Feb. 26, at Farnborough, Hants, the wife of Dr. P. L. Allen—a son.
ARMSTRONG.—On Feb. 28, in London, the wife of Dr. B. P. Armstrong—a son.
CARTER.—On Feb. 26, in London, the wife of Dr. A. B. Carter—a daughter.
DARLEY.—On March 3, at Esher, the wife of Dr. R. D. Darley—a son.
FORBES-WINSLOW.—On Feb. 25, at Douglas, I.o.M., the wife of Dr. V. F. Forbes-Winslow—a son.
HODGKIN.—On Feb. 27, at Oxford, the wife of Dr. Keith Hodgkin—a daughter.
GLASER.—On Feb. 28, at Cambridge, the wife of Dr. E. M. Glaser—a daughter.
HOLLAND.—On Feb. 25, in London, the wife of Dr. C. B. Holland, D.S.C.—a daughter.
JENNINGS.—On Feb. 27, at Shorcham-by-Sea, the wife of Mr. George Jennings, F.R.C.S.—a daughter.
LANDELLS.—On Feb. 27, the wife of Dr. John Landells—a son.
MAYER.—On Feb. 25, at Tarbert, Argyll, the wife of Dr. A. C. Mayer—a son.
PALLOT.—On March 2, in London, the wife of Dr. Michael Pallot—a daughter.
ROBSON.—On March 5, the wife of Dr. J. R. Robson—a son.
SMITH.—On Feb. 26, at Woking, the wife of Dr. Dean Smith, O.B.E.—a daughter.
STORRAR.—On March 5, the wife of Dr. W. Storrar—a daughter.

MARRIAGES

CURRIE—FINDLAY.—On March 3, in London, George Mackay Currie, M.D., to Margaret Wyllis Findlay.
HOUSTON—CRUTTWELL.—On Feb. 23, at St. Albans, John Kenneth Houston, M.B., to Rosemary Christian Cruttwell.
HOTCHKIS—SMOUT.—On March 3, in Edinburgh, Alistair James Hotchkis, to Jean Mary Smout, M.B.
NICHOLSON—CHALK.—On March 1, at Southwell, George Nicholson, M.D., to Eleanor Agnes Chalk.
NICOLL—HARTIGAN.—On Feb. 23, in London, Esmond Douglas Vere Nicoll, M.C., M.R.C.S., to Zita Maxine Hartigan.
ODELL—LICENCE.—On Feb. 26, at Chingford, John Robert Odell, M.B., to Ruth Mary Licence, M.B.
WHITCOMBE—LONGHURST.—On March 5, at Accra, John Leslie Clarence Whitcombe, M.R.C.S., to Aileen Longhurst.

DEATHS

COPLESTONE.—On Feb. 28, at Gorey, Jersey, William Drake Coplestone, M.A., B.CHIR. Camb., aged 69.
KEIGWIN.—On Jan. 27, at Durban, George John Williams Keigwin, L.R.C.P.E.
KER-GIBSON.—On March 3, at Aldershot, Arthur William Ker Gibson, L.R.C.P.E., lieut.-colonel, R.A.M.C. retd.
MARTYN.—On March 1, at Bridgwater, Valentine Cleeve Martyn, M.C., M.R.C.S., aged 64.

Digitized by Google

Notes and News

NEW REMEDY FOR SEASICKNESS

A NEW drug, 'Dramamine,' has given promising results in the prevention and treatment of seasickness. This drug, which is β-diaminoethyl benzohydryl ether 8-chlorotheophyllinate, belongs to the same chemical group as the anti-histamine preparations. The initial research on it was carried out by Dr. Leslie N. Gay and Dr. Paul Carliner, both of Johns Hopkins Hospital, Baltimore. Dramamine was tested last November among 400 passengers aboard a U.S. army transport travelling in heavy seas from New York to Bremerhaven. Of men who were given prophylactic doses, less than 2% became seasick; while of those who received the drug as treatment for seasickness, only 3% were not completely relieved. Despite heavy dosage no toxic symptoms were reported.

The 134 men chosen for the preventive study were given 100 mg. in a capsule as the transport left New York, with the same dose six hours later, and thereafter before each meal and before retiring; this schedule was continued for forty-eight hours, during which no member of the group developed nausea or vomiting, though 2 complained of dizziness. When the drug was discontinued, 41 reported seasickness within 10–18 hours; with resumption of the drug 40 recovered within $^1/_2$–1 hour. Of 123 controls who received sugar capsules, 35 became seasick within 12 hours; when placed on the dramamine schedule, all except 1 were completely relieved within three hours.

Of the group selected for the therapeutic trial, none received the drug at the start of the voyage; altogether 15 became seasick, of whom 12 were immediately relieved by dramamine. A control group of 33 received sugar capsules; 19 whose complaints had been nausea and dizziness were relieved within twelve hours; 14 became progressively worse, complaining of excessive nausea, extreme dizziness, and protracted vomiting, which were completely dispelled within half an hour of an initial dose of dramamine.

Of 195 other men aboard the ship who reported severe symptoms of seasickness, 187 were completely relieved within half an hour of treatment being started. Where men were so ill that they could not retain the capsule, the drug was given per rectum, and, again within half an hour, they were able to retain both fluids and solid food. Plans have been made for further experiments with the drug, including observation of its effect against sickness in landing-craft, small boats, and aircraft.

CARE OF THE OLD IN THEIR HOMES

Dr. E. B. Brooke, medical superintendent of the St. Helier Hospital, Carshalton, has found that requests for the admission of elderly people to hospital are so numerous that the hopes raised by putting a prospective patient on the waiting-list are unwarranted. Speaking at a meeting of the Medical Society for the Care of the Elderly, on Jan. 25, he pointed out that though his hospital has beds, it lacks the staff to man them and to care for additional cases if these were admitted. Part-time nurses or W.V.S. personnel cannot, in his experience, undertake night duty, even where they help by day. In fact, the only place where these patients can get attendance at night is in their own homes; and, since it is impossible to treat them in hospital, the aim must be to bring hospital facilities to the home. When he realised this, his first step was to send a geriatric social worker to see the state of patients whom he had been asked to admit but could not take. The first problem, she found, was to provide suitable meals for patients who had nobody to cook for them. His hospital management committee therefore convened a meeting of various interested bodies, including the county health services, the county social welfare services, the National Assistance Board, and the local (general practitioner) executive council. A standing liaison committee was formed to put into effect the recommendations of the B.M.A. committee on the care and treatment of the elderly and infirm. A hot-meals service —"meals on wheels"—was instituted by the W.V.S. Transport was arranged to bring sitting and lying patients up to the hospital for outpatient examination and physiotherapy; and a laundry service for patients' dirty linen was set up, the hospital serving as a headquarters for collection and delivery. The geriatric social worker got into regular touch with district nurses, the home-help service, Red Cross workers, and W.V.S. occupational therapy teachers of the home-bound. She has also hunted out people who are willing to shop for the aged sick and to visit them from time to time. In many cases it is possible to arrange for a service of "patient-watchers" among the neighbours. This scheme is only possible where the general practitioner is willing to coöperate, but once his support is forthcoming the motto of the domiciliary service is "Everything possible, short of admission to hospital."

During the first three months the new service helped 100 patients who could not otherwise have been cared for at home, yet for whom there were no hospital beds. Among her other duties, the geriatric social worker decides the order of priority of cases for whom a bed may become available, after discussing their social and medical needs with the physician. Two types of patient are usually given priority: those who might benefit quickly by medical treatment, and those who are very ill and living in unsuitable home conditions. Though the service is still imperfect, it is an advance on the practice of allowing patients to remain at home without any help, or of putting their names on a meaningless waiting-list.

Mrs. Pullinger, the hospital geriatric social worker, finds she is welcomed by the relatives of patients and by the general practitioners. The care given by the district nurses helps patients greatly, and they value the meals-on-wheels service. Dr. Eneas McIntyre, medical officer of health for Sutton and Cheam, said that, now the old relieving officer has gone, there is nobody to whom cases of difficulty can be referred. The borderline type of infirm old person needing care and attention is a great problem, for the National Assistance Act does not always cover his case. Dr. Marjory Warren urged that the social worker should become attached to the almoner's department.

REVIEW OF CONVALESCENT HOMES

UNDER the National Health Service Act, regional hospital boards are responsible for reablement that includes medical treatment, while local health authorities have the power to cater for those needing little or no more than rest, good food, fresh air, and regular hours. On this basis regional boards have been asked by the Ministry of Health to determine, in consultation with local health authorities, which of these two bodies should pay the cost of health service patients' stay in "outside" homes which were not transferred to the Minister under the Act. Boards are warned against a predatory approach to the review; for local health authorities have a need of convalescent accommodation which, if less obvious, is no less real than that of hospitals. On the other hand homes which provide treatment, but of an unsatisfactory standard, should not be classed as non-treatment homes: instead they should become the responsibility of the board, which should urge these homes to raise their standard. The Minister's view is that admission to homes of either class should take place only on the recommendation of a doctor, though not necessarily of a hospital doctor; and "whatever machinery the Board adopts for the placing and admission of non-hospital convalescent patients, they should not automatically be placed below ex-hospital patients on any waiting list."

THE GUY'S DENTAL SCHOOL

THE annual clinical meeting, held at Guy's Hospital Dental School last Saturday, was attended by some 400 Guy's men. A tour of the school revealed many improvements. The prosthetics laboratory has been modernised, and fitted, like most of the rest of the school, with fluorescent lighting. The conservation room, with a complete dental unit for each chair, must be the envy of other teaching hospitals, and instrument cabinets are to be set between the chairs so that the patients will have more privacy than is usual in hospitals and clinics in this country.

At the moment, there are more than 300 dental students, 8 of whom are women. The high standard of their work was reflected in the various displays during the meeting. A feature of the dental training at Guy's has always been the emphasis placed on the close relation between the teeth and the rest of the body. This emphasis has been increased by the recent creation of the department of dental medicine under Prof. M. A. Rushton and that of preventive dentistry under Mr. G. J. Parfitt.

Clinical cases of wide range were demonstrated, and operating sessions were held by Mr. Nils Eckhoff, Mr. S. H. Wass, Mr. Patrick Clarkson, and Mr. W. Kelsey Fry in the surgical theatres. Of the films exhibited two deserve special

Digitized by Google

mention—*Movements of the Tongue in Speech* and *Dental Anæsthesia*. The first is in colour and shows an edentulous patient, with the right cheek surgically removed, making the movements necessary to produce letters, words, and sentences. The second, shown publicly for the first time, has been made by Imperial Chemical Industries and was introduced by Dr. W. S. McConnell, anæsthetist to the hospital; it is worthy of wide circulation in the medical and dental professions.

A new development is the use for teaching purposes of coloured photomicrographs (made by either the Kodachrome or Ektachrome process) for projection instead of either the actual preparations or black-and-white slides. It is hoped to make coloured photographs of all interesting specimens now in the possession of the school. Coloured photographs are also used extensively for clinical records, and a special outfit, consisting of a modified Leica camera with synchronised electron flash-tubes, has been developed for this purpose.

The dental research laboratory is carrying out work on the detailed structure of enamel and on the variations of salivary pH values. The research is purely chemical at the moment, but it will be extended shortly to physical investigations with the electron microscope and electron diffraction microscope. Research is also in progress in the department of preventive dentistry on the significance of the lactobacillus-count, and on the effectiveness of urea-ammonium toothpastes in decreasing the incidence of dental caries.

The visitors were grateful to the subdean of the hospital, Mr. F. S. Warner, for the admirable arrangements and warm hospitality.

ADAPTATION OF E.M.S. HUTS

SUGGESTED plans for converting E.M.S. huts to peace-time hospital purposes were published in a supplement to the *Monthly Bulletin of the Ministry of Health* for February, 1946; and a further set of plans has now been issued. Three of these new plans cover the use of E.M.S. huts to form an outpatients' hostel, to be used by patients needing to stay in or near the hospital for a few days' investigation or treatment but not requiring to be in the wards.

FILM ON THE PROLAPSED DISC

Mr. J. E. A. O'Connell, with the assistance of the St. Bartholomew's Hospital photographic department, has produced a film dealing with the diagnosis and operative treatment of prolapsed intervertebral disc. The film, intended primarily for undergraduate instruction, succeeds in its purpose. The clinical section, which can be shown separately, is especially lucid; the only criticism is that a few close-ups of the patient's back during movement would have been helpful. The operative section again shows in an orderly fashion the successive stages of the procedure; the detail in the depth of the wound is not seen, but this is probably not of importance in such a teaching film. A particularly valuable part is that showing postoperative reablement in the physiotherapy department—an essential feature of treatment which the student might easily overlook. The running-time is 30 minutes.

EXCHANGE HOLIDAYS

SINCE the war, many people who wish to spend their holidays abroad have been hindered from doing so by the high cost of hotels and restaurants. It is not easy for the stranger to find more modest yet suitable accommodation; yet many flats and houses are empty while their owners are on holiday.

L'Echange Touristique International, a non-profit-making association, helps to arrange these exchanges of homes. Those who wish to find out more about this scheme should write to the secretary of the association, 91, Bd. Malesherbes Paris (8e), France, with an international reply-paid stamp. They will be sent a questionary in which they will be able to set out their own needs and details of the accommodation they are able to offer to a foreign member of the society. The scheme is in accordance with Bank of England control regulations, provided that no money passes between the parties concerned, and that there is no monetary consideration for the provision of such accommodation, including the settlement of bills for household supplies.

University of Oxford

On Feb. 26 the following degrees were conferred:

D.M.—M. A. Partridge, A. P. Meiklejohn, George Gordon, J. A. L. Leeming.*

B.M.—V. J. E. Davies.*

* In absentia.

University of Cambridge

The degree of M.A. has been conferred on Sir Alan Rook, senior health service officer of the university health service. The following degrees have also been conferred:

M.D.—C. H. Hoskyn, D. G. R. Fox.

M.B., B.Chir.—W. I. N. Kessel,* R. V. Grange,* T. C. Langdon,* D. N. Phear, J. E. Naylor, P. C. J. Nicholl, M. I. M. Pines.

* By proxy.

Royal College of Physicians of London

Dr. A. P. Thomson will deliver the Lumleian lectures on Tuesday and Thursday, April 5 and 7, at 5 P.M. at the college, Pall Mall East, S.W.1. He is to speak on Problems of Ageing and Chronic Sickness.

Royal College of Surgeons of England

On Wednesday, March 16, Mr. A. D. Marston, dean of the faculty of anæsthetists, will deliver the first Clover lecture. He is to speak on Joseph Clover, his Life and Achievements. On Wednesday, March 23, Dr. Frank E. Adair, surgeon to the Memorial Hospital, New York, will give the Moynihan lecture on the Results of Surgery in the Treatment of Breast Cancer. Both lectures will take place at 5 P.M.

Course on Rheumatism

The Empire Rheumatism Council is holding a course at the Apothecaries' Hall on Friday, Saturday, and Sunday, April 8, 9, and 10. Further particulars will be found in our advertisement columns.

The Blind in the Modern World

Representatives from nineteen countries are taking part in the assembly of workers for the blind, to be held from Aug. 3 to 13 at Merton College, Oxford, which is to discuss this topic. Further information may be had from the National Institute for the Blind, 19, Buckingham Street, London, W.C.2.

Chesterfield Medal

The examination in dermatology for this medal will be held at St. John's Hospital for Diseases of the Skin, 5, Lisle Street, London, W.C.2, on Monday, Tuesday and Friday, April 4, 5, and 8. Further particulars may be had from the dean of the institute of dermatology at the hospital.

Medical Delegation to Poland

Prof. W. J. B. Riddell, Prof. D. M. Dunlop, Dr. G. S. Wilson, Dr. Marc Daniels, and Mr. G. H. Macnab are visiting Poland under an exchange scheme organised by the British Council and the Polish ministry of health. The first part of the exchange took place last month when five Polish professors visited London and the provinces.

Informing the Public

The public-health department of the Middlesex County Council are holding a symposium at the London School of Hygiene, Keppel Street, W.C.1, on Monday, March 14, beginning at 10 A.M., on the principles and technique of informing the public.

World Health Organisation

Of 58 member countries 34 have requested W.H.O. assistance for advisory and demonstration services, and $716,045 has been allocated by the director-general for such services and for fellowships during the first quarter of 1949. W.H.O. assistance will take the form of consultative advice from experts attached to the health administrations, sending of demonstration teams to teach the latest techniques in disease control, and visits by lecturers. The executive board has approved a total of $1,403,000 for these services during the year: in addition, there is available a $1,000,000 special UNRRA fund which is being used for joint UNICEF-W.H.O. programmes.

The 1948 budget of W.H.O. amounts to $4,860,223, of which only $3,180,609 has so far been collected, from 32 of 70 contributing countries.

The regional office for the Eastern Mediterranean will open in Alexandria on or about July 1, with Sir Aly Towfik Shousha, Pasha, as director. The Egyptian government has placed the site and building at the disposal of W.H.O. for nine years at a nominal rent of 10 piastres a year. As from March 1 the Pan-American Sanitary Bureau will serve as the regional office of W.H.O. for the Western Hemisphere. This is an initial step towards eventual integration of the Pan-American Sanitary Organisation into W.H.O.

Digitized by Google

Bristol Medical Reunion

The dinner will be held on Wednesday, April 20 (not April 30). Particulars may be had from Dr. Richard Clarke, Harley Lodge, Clifton Down, Bristol, 8.

National Hospital, Queen Square

Owing to illness Prof. J. Lhermitte's lecture on Visual Hallucinations, which was to have been given at the institute of neurology on March 17, has been cancelled.

Royal Photographic Society

The second part of the annual exhibition, which the society is holding at 16, Princes Gate, London, S.W.7, this autumn, will include a medical section which will be open from Oct. 8 to 26.

Medical Sickness Finance Corporation

This body has been incorporated as a private limited company to give hire-purchase facilities to doctors and dentists for the purchase of cars and equipment. The corporation is a subsidiary of the Medical Sickness Annuity and Life Assurance Society Ltd., and the offices are at 7, Cavendish Square, London, W.1. The chairman is Sir Cecil Wakeley.

Markle Foundation Scholarships

This year two of the thirteen scholarships awarded by this foundation to qualified men and women who wish to remain in academic medicine have gone to British graduates. Dr. J. D. Green has been given a grant in anatomy and physiology tenable at Wayne University College of Medicine, Detroit, and Dr. D. R. Wilson in internal medicine at the University of Alberta faculty of medicine, Edmonton.

Lost Drugs

In response to the Pharmaceutical Society's request that they should not broadcast the names of lost drugs the B.B.C. have decided to discontinue broadcasting police messages about lost or stolen drugs within the Metropolitan police district, except where there is real danger to life or when drugs or poisons have been purchased in mistake for some harmless medicine. The society's objection was based on the fact that the name of the drug might disclose the doctor's treatment to the patient and also that the repetition of words like phenobarbitone made less responsible listeners regard such drugs as a joke.

Visitors Studying Social Pædiatrics

Some 47 doctors and nurses from 14 countries of Europe and the Middle East, holders of UNICEF fellowships, are in the United Kingdom for three months, during which they will study social pædiatrics, under arrangements made by the Ministry of Health and the British Council. Groups are working at Birmingham, Bristol, Liverpool, Manchester, Newcastle, Edinburgh, and Glasgow. The visitors will assemble at Oxford for ten days from March 27, and the last part of the visit, from May 29 to June 8, will be spent in London.

Ophthalmic Practitioners' Fees

The Ministry of Health announces that from April 1 the fee normally payable to an ophthalmic medical practitioner for testing sight under the supplementary ophthalmic services, will be reduced from the present £1 11*s.* 6*d.* to £1 5*s.* A Ministry letter informing executive councils of this decision says that the existing fee " was based on the assumption that the average time taken to complete such a test was half-an-hour. The Minister has, after discussion with representatives of the profession, come to the provisional conclusion that the average time is in fact less." The new fee will be subject to review in the light of a proposed investigation into the times actually taken.

Society of Medical Officers of Health

Under the presidency of Dr. R. M. Galloway, the county-borough group will hold their annual meeting and conference at Low Wood, Windermere, from May 6 to 9. Dr. C. Metcalfe Brown and Dr. F. Hall will speak on the Working of the National Health Service Act, 1946, Dr. W. Rees Thomas on Mental Health Service Responsibilities of Part III Authorities under the Act, Mr. A. W. G. and Mrs. Irene Ewing on the Care of the Deaf, Prof. I. G. Davies on the Training of Health Visitors, and Prof. Andrew Topping on Medicine—Social and Antisocial—in West Africa. The hon. secretary is Dr. J. Greenwood Wilson, City Hall, Cardiff.

International European Society of Hæmatology

This society is holding a meeting in Montreux, Switzerland, on Sept. 15, 16, and 17. Hæmolytic anæmias, and Changes in the Blood-proteins in Blood Dyscrasias, have been proposed as subjects for the main discussion. Further information may be had from Dr. A. Piney, 152, Harley Street, London, W.1.

Prof. R. A. Peters, F.R.S., is lecturing for the British Council in Milan, Pavia, Padua, Bologna, Rome, and Naples.

Dr. Fraser Brockington has been appointed a member of the Advisory Council on the Welfare of Handicapped Persons which the Minister of Health has set up under the chairmanship of Lord Rushcliffe.

Mr. Hugh Linstead, M.P., secretary of the Pharmaceutical Society of Great Britain, has been elected a foreign corresponding member of the Academy of Medicine of France.

Appointments

BRIGDEN, W. W., M.A., M.B. Camb., M.R.C.P.: asst. physician London Hospital.

Ministry of Health:

M.O.:
BERRY, W. T. C., M.A., M.B., D.T.M. & H.
ELEY, A. J., M.A., M.B. Lond.
PURVIS, M. S., O.B.E., M.D. Glasg.

Northern Regional Hospital Board:

READ, R. A., M.B. Edin., D.P.H.: asst. administrative M.O.
RICHARDS, R. L., M.B. Aberd., D.O.M.S.: ophthalmologist.

United Cardiff Hospitals:

LLOYD, K. N., M.B. Lond., M.R.C.P.: physician i.c. department of physical medicine.
O'FARRELL, A. W. J., M.B. N.U.I., D.P.H.: asst. radiotherapist.

Diary of the Week

MARCH 13 TO 19

Monday, 14th

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Dr. Denis Williams: Electro-encephalography. Dr. I. Muende: Warts.

Tuesday, 15th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Prof. H. P. Himsworth: Syndrome of Diabetes Mellitus. (First Oliver-Sharpey lecture.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. A. C. Roxburgh: Cutaneous Syphilis.

Wednesday, 16th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. A. D. Marston: Joseph Clover, his Life and Achievements. (Clover lecture.)

HARVEIAN SOCIETY OF LONDON
8.15 P.M. (26, Portland Place, W.1.) Mr. W. B. Gabriel: Common Diseases of the Rectum and Anus.

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. C. W. McKenny: X-ray Technique.

MIDDLESEX COUNTY MEDICAL SOCIETY
3 P.M. (Ashford Hospital, London Road, Ashford.) Demonstration of cases.
5 P.M. Dr. J. A. Brocklebank, Dr. K. D. Keele: Angiocardiography in the Diagnosis of Congenital Heart Disease.

Thursday, 17th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Professor Himsworth: Syndrome of Diabetes Mellitus. (Last Oliver-Sharpey lecture.)

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE
7.30 P.M. (Royal Army Medical College, Millbank, S.W.1.) Laboratory meeting.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Psychiatry lecture-demonstration.

Friday, 18th

WEST LONDON MEDICO-CHIRURGICAL SOCIETY
7.30 P.M. (South Kensington Hotel, 41, Queen's Gate Terrace, S.W.7.) Dr. Keith Simpson: Foul Play.

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. J. Browning Alexander: Acute Pericarditis.

FACULTY OF RADIOLOGISTS
2.15 P.M. (Royal College of Surgeons.) Joint meeting with R.S.M. radiological section. Prof. R. A. Willis, Prof. A. S. Johnstone: Tumours of the Kidney.
8.15 P.M. (1, Wimpole Street, W.1.) Mr. T. Twistington Higgins, Mr. R. Ogier Ward, Miss M. D. Snelling: Tumours of the Kidney.

Digitized by Google

HISTORICAL BUILDING
DES MOINES, IOWA

THE SYNDROME OF DIABETES MELLITUS AND ITS CAUSES*

H. P. HIMSWORTH
M.D. Lond., F.R.C.P.
PROFESSOR OF MEDICINE, UNIVERSITY OF LONDON; DIRECTOR OF THE MEDICAL UNIT, UNIVERSITY COLLEGE HOSPITAL, LONDON

THE history of modern knowledge is concerned in no small degree with man's attempt to escape from his previous concepts. Within the present century we have seen physics liberated from the cramped philosophy of a rigid causality to the more fluid concept of probability. We are now witnessing a similar liberation of medical thought by the substitution of syndromes for "disease entities" as the units of illness. Implicit in the concept of a disease entity is the idea that any particular illness has a specific cause, which, though its action in the body may be modified by circumstances, is an essential and invariable prerequisite for the development of the illness in question. The syndrome, on the other hand, has its philosophical basis not in specific disease factors but in a chain of physiological processes, interference with which at any point produces the same impairment of bodily function. The same syndrome may thus arise from many different causes. This newer view inspires a far more catholic concept of ætiology and renders pointless many existing controversies. But the revision of medical thought entailed by its application has hardly begun. It is my purpose to apply these considerations to the syndrome of diabetes mellitus.

Ten years ago I attempted to present to this college a general view of the chain of processes concerned in the regulation of carbohydrate metabolism. From these considerations the following concept emerged[23]:

The rate of utilisation of carbohydrate by the tissues is governed by the height of the blood-sugar and in any particular circumstances this is adjusted to the level which comes nearest to ensuring an adequate rate of utilisation. Thus, when the ability of the tissues to use carbohydrate is impaired, as by deficiency of insulin, impairment of insulin action, or interference with intracellular oxidation, the head of pressure of blood-sugar is raised, thereby accelerating the disposal of sugar by the tissues. Conversely, when the ability of the tissues to dispose of carbohydrate is increased, the head of pressure is adjusted to lower levels and excessive utilisation of carbohydrate prevented. The ability to utilise carbohydrate is inherent in the tissues, but the rate of utilisation is accelerated by the insulin secreted in response to hyperglycæmia, and retarded by factors secreted by the anterior pituitary gland. The agent of these adjustments of blood-sugar is the liver, which stores sugar as glycogen when the needs of the tissues are satisfied, but when they are unsatisfied liberates glucose into the blood either by glycogenolysis or by new formation from non-carbohydrate sources. The liver is influenced in these reactions by hormones from the anterior pituitary gland which are secreted in response to carbohydrate starvation in the tissues. When such hormones are present in excess, glycogenolysis and new formation of sugar are accelerated; when the quantity of hormones is diminished, these processes are retarded. Finally, the object of these efficient and sensitive adjustments of the blood-sugar level is to ensure an adequate supply of glucose to the brain, for, so far as is known, the brain utilises only carbohydrate and is immediately dependent on the blood-sugar for its supplies.

It is evident that interference in this system of processes could occur at many points and lead, in each case, to the syndrome we recognise as diabetes mellitus. But before such possible interferences are discussed the hypothesis must be reconsidered in the light of recent knowledge.

Mode of Action of Insulin

In the path of intracellular carbohydrate metabolism there are certain obligatory stages through which the metabolic stream must pass without option of circumvention. One of the most important of these occurs at the very beginning in the reaction by which glucose, under the influence of adenosine triphosphate, is turned into glucose-6-phosphate. This reaction is catalysed by the enzyme hexokinase. Once glucose-6-phosphate has been formed, synthesis of glycogen and the whole chain of carbohydrate oxidation become possible even to diabetic animals. Cori and his school[8 10 54] have now shown that, in vitro, the vital hexokinase reaction is inhibited by anterior pituitary extracts (A.P.E.); that tissue preparations made from animals previously injected with such extracts show similar inhibition; and, further, that this inhibition is counteracted by insulin. Muscle extracts made from alloxan-diabetic rats show the same impaired ability to use glucose as do extracts from normal rats injected with A.P.E.; but, if the animals are previously injected with insulin, the hexokinase activity is normal. Such inhibition is enhanced by adrenocortical extracts, and this also is removed by insulin. Insulin, however, does not directly facilitate the activity of hexokinase; it simply removes any A.P.E. inhibition that is present. These results have been confirmed by Reid, Smith, and Young,[56] who have also confirmed the observation that, though A.P.E. capable of producing diabetes on injection into dogs may show no hexokinase inhibitory action in vitro, tissue extracts from animals so injected show such inhibition. It remains to show that Cori's in-vitro results are applicable to the living animal as a whole. The evidence was previously available.

The action of insulin in the peripheral tissues was conclusively demonstrated by Mann and Magath[43] and by Burn and Dale.[5] The former showed in dogs that, after hepatectomy, insulin produced a rapid fall of blood-sugar; the latter showed that it accelerated the disappearance of infused sugar in decapitated eviscerated preparations. Soon after the discovery by Houssay that hypophysectomy ameliorated pancreatic diabetes it was found that injection of A.P.E. into normal animals produced insensitivity to insulin.[9 34 74 75] In general this failure of insulin to depress the blood-sugar level in animals so treated was attributed to their livers either being unable to store sugar or masking the depressant action of insulin by excessive liberation of glucose. That this was not the whole truth was indicated by Marks,[44] who showed that decapitated eviscerated preparations made from cats previously injected with A.P.E. formed less muscle glycogen than normal under the action of insulin. The peripheral action of A.P.E. was investigated by Himsworth and Scott,[28] whose results have been confirmed by Bennett and Roberts.[4] A method was devised by which the liver of unanæsthetised rabbits could be painlessly and instantly excluded from the circulation.[22] Such preparations behave exactly like hepatectomised animals, the blood-sugar falling steadily and death occurring in hypoglycæmia in an average of 292 ± 70 min. If, immediately after exclusion of the liver, 1 unit of insulin is injected intravenously, the fall of blood-sugar is accelerated and death occurs at 90 ± 14 min. (fig. 1). But, on repeating these experiments on rabbits previously treated with A.P.E., a striking difference was observed. The "spontaneous" fall of blood-sugar proceeded at practically the same

* Oliver-Sharpey lectures to the Royal College of Physicians, March 15 and 17, 1949.

Digitized by Google

rate as in the uninjected animal after exclusion of the liver, but insulin now did not accelerate this fall.

It is thus evident that, both in the animal as a whole and in vitro, A.P.E. inhibits the action of insulin in accelerating the disposal of sugar by the peripheral tissues. What requires further consideration is why A.P.E. does not inhibit the "spontaneous" disposal in the hepatectomised animal. Originally this was interpreted to mean that utilisation of carbohydrate might proceed through mechanisms which did not require the aid of insulin.[28] Cori's work suggests that in a sense this is true. Brain hexokinase, unlike muscle or liver hexokinase, is relatively insusceptible to A.P.E. inhibition[8]; insulin has little, if any, effect on brain metabolism[16 37]; and in animals deprived of insulin by pancreatectomy the brain continues to oxidise carbohydrate at a practically normal rate.[33] Further, even in muscle and liver the inhibition of hexokinase activity by A.P.E. is not complete. The relatively normal "spontaneous" fall of blood-sugar in hepatectomised animals previously injected with A.P.E. may well be the expression of carbohydrate utilisation by tissues whose hexokinase is relatively insusceptible to such inhibition and to the residual activity in those tissues which are more susceptible. The corollaries of this view are that insulin is primarily required for those tissues in which A.P.E. readily produces inhibition and, further, that some degree of such inhibition should be present, even in non-diabetic animals, if insulin is to act. These results are in accord with the views of Russell[60 61] that the anterior pituitary gland acts on carbohydrate metabolism primarily by restricting utilisation in the tissues. Her views are based on the observations that in hypophysectomised animals oxidation is increased, muscle glycogen disappears more rapidly, and, in eviscerated preparations made from such animals, more glucose is required to maintain a normal blood-sugar level.

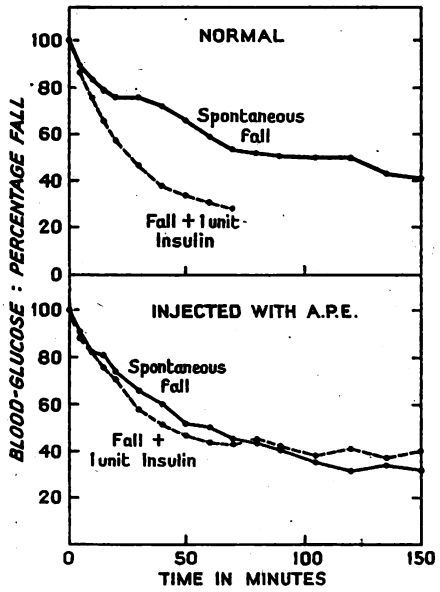


Fig. 1—Percentage fall of blood-glucose level in rabbits in which at 0 min., the liver was excluded instantaneously, painlessly, and without anæsthesia, by method described[32]: showing that A.P.E inhibits action of insulin in peripheral tissues.[18]

Insulin and A.P.E. thus appear as regulators of those basic reactions which dispose of glucose, and, their actions being most pronounced in the tissues which are the major consumers of glucose, as agents admirably adapted to cope respectively with plethora and scarcity of carbohydrate. From this point of view several observations fall into place. Carbohydrate deprivation diminishes insulin sensitivity and glucose tolerance in a manner similar to A.P.E. extracts; but this diminution is not seen in hypophysectomised rabbits.[27] Such deprivation also decreases the ability of the peripheral tissues to dispose of glucose.[18 42] Well-marked differences occur between the effects of pancreatectomy in different species. Over fifty years ago Minkowski and Weintraud[46] suggested that these differences were related to feeding-habits, diabetes being severe in carnivora, who in their natural state are subject to alternating periods of plenty and scarcity, but mild in herbivora, whose feeding-habits are more settled. We can visualise the anterior pituitary gland as being concerned with adaptation to starvation, by retarding the utilisation of sugar in the tissues, preventing the accelerating effect of insulin, and facilitating the supply of sugar from the stores of liver glycogen and non-carbohydrate sources. Insulin, on the other hand, is concerned with inhibiting these reactions and thus maintaining the utilisation of glucose, and, its secretion being elicited by hyperglycæmia, in promoting the storage of any sudden influx of carbohydrate.

Thus at any particular time, even in the normal animal, the rate of glucose disposal depends on the balance between the anterior pituitary factor and insulin. In the absence of insulin the inhibition of glucose utilisation, consequent on A.P.E.-like factors, would be unchecked, the rate of such utilisation by the tissues would decrease, and a state of relative carbohydrate starvation in the tissues would develop. Diabetes mellitus consequent on insulin lack now appears as an extreme example of carbohydrate starvation, the manifestations of excessive anterior pituitary function in this condition as an inevitable exaggeration of a physiological response, and the beneficial effect of insulin therapy as the result of breaking through the inhibition due to anterior pituitary factors in the tissues susceptible to its action.

But these new findings should not blind us to the fact that insulin and A.P.E. are essentially concerned not with basic but with regulating mechanisms. The mass action effect of the blood-sugar level still stands in a more fundamental relation to carbohydrate metabolism. Even in the absence of insulin, a high blood-sugar level can ensure utilisation of carbohydrate at a normal rate.[64] If we may assume an A.P.E. inhibition in the tissues of depancreatised dogs similar to that which Cori has demonstrated in the muscles of rats with insulin deficiency due to alloxan diabetes, it seems that a high blood-sugar level can overcome this inhibition. The advantages to the organism of raising the blood-sugar level when insulin is lacking are so evident, and such elevation occurs so consistently, as to compel the idea of compensation. And some such compensation seems to be a physiological necessity. By itself A.P.E. provides only a crude response to starvation; for, though it retards the utilisation of glucose predominantly in tissues like muscle, which can use other substances, it is not without a similar, if milder, effect in tissues such as the brain, to which glucose is a vital necessity.[8] Hyperglycæmia, by overcoming mild degrees of inhibition, would ensure a continuing adequate rate of glucose utilisation in tissues like the brain under conditions in which an economical retardation was being exerted elsewhere. Further, however appropriate the metabolic state produced by A.P.E. to the starving animal, it may be quite inappropriate when starvation is relieved and a sudden inrush of glucose requires disposal. An increased alimentary hyperglycæmia, even with no abnormal increase of insulin secretion, renders this possible.

There remains, however, one outstanding question—the nature of the linkage by which the needs of the tissues are communicated to the anterior-pituitary-liver mechanism which effects the necessary adjustments of blood-sugar level and redistribution of metabolic priorities. There is no direct evidence on this point, but since such a mechanism was postulated two linkages of this type have been recognised. Verney[69] has demonstrated that certain centres in the hypothalmus are susceptible to osmotic changes and react by altering

Digitized by Google

the rate of secretion of posterior pituitary hormones. The production of thyrotropic hormone by the anterior pituitary gland appears to be determined by the concentration of circulating thyroid hormone. It does not seem unreasonable to imagine that "centres" in the brain may be found which react to alterations in their carbohydrate metabolism by changing the output of the relevant anterior pituitary hormones. Then, perhaps, piqûre diabetes will acquire a new significance.

The demonstration that insulin can be directly inhibited provides a further stimulus to the idea that factors other than deficiency of insulin may cause the syndrome of diabetes mellitus in man. Such cases, if they exist, would manifest relative insensitivity to insulin. It is therefore necessary to consider the question of insulin sensitivity in human diabetes.

Insulin Sensitivity

MEASUREMENT OF INSULIN SENSITIVITY IN MAN

Shortly after the introduction of insulin into medical practice it became clear to clinicians that some diabetic patients were relatively refractory to its influence. In general, such differences have been regarded as the result of complicating factors which superimposed a relative resistance to insulin upon the basic disease of diabetes mellitus. Undoubtedly, temporary resistance of this nature can occur in any diabetic patient from a wide variety of conditions—e.g., infection, thyrotoxicosis, and unsuitable diets [11]—but it is difficult to explain on this basis the persistent differences in insulin sensitivity between apparently uncomplicated cases of diabetes mellitus. As a result the concept arose of insulin-sensitive and insulin-resistant types of diabetes mellitus, and Radoslav [55] tried to obtain evidence in its support by measuring the rate at which insulin depressed the blood-sugar in different patients. He failed because it was not then known that the effect of insulin varied with the height of the blood-sugar [63]; but the Viennese school pursued the idea and gathered an impressive body of evidence, which is summarised in Falta's monograph of 1936.[14] In Falta's sensitive type each unit of insulin prevented the excretion of several grammes of urinary sugar, hypoglycæmia was readily produced, and withdrawal of diet and insulin was speedily followed by profuse glycosuria and ketosis. In his resistant diabetic many units of insulin were required to prevent the excretion of each gramme of urinary sugar, excess of insulin seldom produced hypoglycæmia, and withdrawal of therapy for 24 hours rarely led to more than a trace of glycosuria. The results of these tests, however, were not always in agreement, nor were they consistently related to any clinical type. Nevertheless, they seem to indicate a genuine difference between patients.

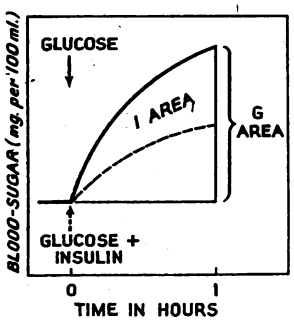


Fig. 2—Glucose-tolerance and insulin-glucose curves, showing glucose-tolerance area (G) and insulin area (I).

In this country a different line of work led to similar conclusions. The efficiency with which insulin acts in a normal person is determined by the variable of insulin sensitivity, which is proportional to the carbohydrate content of the diet.[19] The possibility of two types of diabetes, one due to lack of insulin and one to insensitivity to insulin, was thus raised. A test to measure insulin sensitivity was accordingly devised [21]: a standard dose of glucose is given by mouth, followed immediately by a standard dose of insulin injected intravenously.

When the oral glucose-tolerance test or the insulin-glucose test is carried out under standard conditions, the area subscribed by the blood-sugar curve above the fasting level [23] is approximately constant for that person. Clearly the difference between the area of the glucose-tolerance curve (fig. 2, G area) and the insulin-glucose curve area is a measure of the effect of the injected insulin (fig. 2, I area). Now the height of the blood-sugar level determines the degree to which a particular dose of insulin will depress the blood-sugar; so before one can interpret the insulin-glucose test a method of estimating this influence is required. By measuring the effects of a standard dose of insulin on blood-sugar tolerance curves of different heights, under constant conditions of insulin sensitivity, it was found that the suppression of alimentary hyperglycæmia by insulin was directly proportional to the size of the blood-sugar curve on which insulin acted. In other words, the ratio insulin area to glucose area (I/G ratio) was constant when the insulin sensitivity was constant.[29]

The changes in the insulin-glucose test consequent on changes in insulin-sensitivity were then investigated. Such sensitivity can readily be reduced by restricting dietary carbohydrates and the reduction is manifested by higher and longer glucose-tolerance curves and also by similar changes in the insulin-glucose curve. On comparing the two curves it is found that, when changes in the glucose-tolerance curve are brought about by changes in dietary carbohydrate, the suppression of hyperglycæmia shown by the insulin-glucose test is no longer proportional to the height of the blood-sugar. The insulin area in fact remains approximately constant, so that the I/G ratio declines progressively as the sugar-tolerance curves become higher and longer. The I/G ratio thus provides a measure of insulin-sensitivity which is independent of the height of the blood-sugar, and, as such, is applicable to the investigation of insulin sensitivity in diabetics.[29]

INSULIN SENSITIVITY IN DIABETICS

When we speak of insensitivity to insulin in a diabetic we mean insensitivity which persists in the controlled patient without intercurrent illness and taking a high carbohydrate diet, for it is well known that temporary insensitivity may be induced by infection, ketosis, and carbohydrate starvation.

When the insulin-glucose test was applied to human diabetics, two distinct types of response were obtained.[21] In one—the sensitive type—insulin came into action

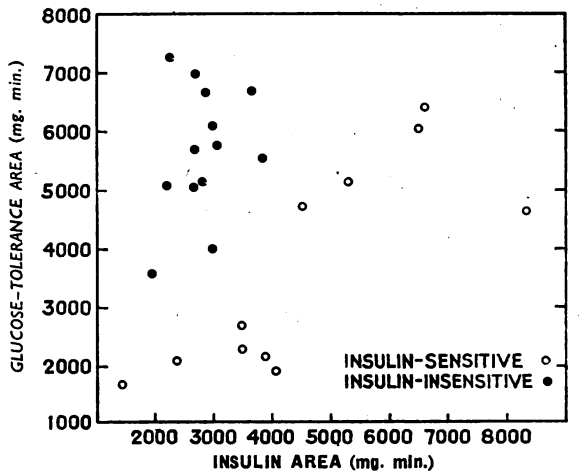


Fig. 3—Glucose-tolerance area plotted against insulin area, showing that, in sensitive diabetic patients, insulin area increases with glucose-tolerance area, whereas in insensitive cases it remains about the same.[21]

Digitized by Google

rapidly and suppressed the rise of blood-sugar which should have followed the ingestion of glucose. In the other—the insensitive type—insulin came into action slowly and weakly, and there was little suppression of alimentary hyperglycæmia.

Measured under the standard conditions of the test the I/G ratio for healthy persons was about 1. For those diabetics classed as insulin-sensitive the I/G ratio averaged 1·34 (S.E. 0·12; S.D. 0·39); for those classed as insensitive it averaged 0·51 (S.E. 0·03; S.D. 0·11). The insulin-glucose test thus sharply differentiates two groups of diabetics on the basis of their sensitivity to insulin.[30] On charting the insulin area against the corresponding glucose-tolerance area (fig. 3) it will be found that in sensitive diabetics the insulin area increases with the degree of alimentary hyperglycæmia, just as it does in normal people under similar standard conditions. In insensitive diabetics, on the other hand, the insulin area alters relatively little, despite wide differences in alimentary hyperglycæmia, just as it does in normal people whose insulin sensitivity is varied by altering the composition of the diet. These are exactly the responses which would be foretold if sensitive diabetes were due to lack of insulin, and insensitive diabetes not to lack of insulin but to insensitivity to insulin.[30]

Other facts point in the same direction. The impaired glucose-tolerance curve of the sensitive diabetic is converted by insulin into an essentially normal insulin-glucose curve, but that of the insensitive diabetic is not. Sensitive diabetics react to increase of dietary carbohydrate by increase of insulin sensitivity; insensitive diabetics do not.[30] In normal people and sensitive diabetics insulin conspicuously increases the rate at which the peripheral tissues remove blood-sugar; in insensitive diabetics this action is greatly impaired.[21] Lastly, Ricketts and Stare [59] showed that, though insulin will increase the rate of oxygen consumption by minced skeletal muscle from uncontrolled diabetic patients who are readily responsive to insulin, it will not do so in similar preparations from the muscles of diabetics who do not readily respond.

Broadly speaking, patients giving the insulin-sensitive response to the insulin-glucose test tend to be young and thin, with healthy arteries and a normal blood-pressure; in them the disease is severe and of sudden onset but readily responsive to insulin; they rapidly develop ketosis, and slight excess of insulin produces hypoglycæmia. The type with the insensitive response tends to be older and obese, with arteriosclerosis and a high blood-pressure; in him the disease is milder, of insidious onset, and often surprisingly insusceptible to insulin; ketosis rarely develops, and he can tolerate a large excess of insulin without symptoms.

We have seen that diabetics fall into two distinct groups according to their sensitivity to insulin, and intermediate degrees of sensitivity between the frankly sensitive and the frankly insensitive are rare. But, when the insulin sensitivity of normal people is tested, it is found that such intermediate degrees occur in the apparently healthy and are found with increasing frequency in the older age-groups.[31] It appears that insensitivity to insulin must exceed a certain degree for diabetes to develop. As a consequence all insensitive diabetics have high degrees of insensitivity.

PRIMARY DEFICIENCY OF INSULIN

The only source of insulin that we know is the islet tissue of the pancreas; and pancreatectomy, or destruction of the β cells of the islets, is invariably followed in susceptible animals by the development of diabetes. Until recently the only similar data on man were from those cases in which tumours had destroyed the pancreas, and such were necessarily subject to reservation because of the general illness and cachexia of these patients. But, now that the difficulties of total pancreatectomy in man have been surmounted, human cases suitable for metabolic studies have become available, and it is evident that pancreatic diabetes in man is surprisingly mild when judged by insulin requirements. Thus in a typical case [58] only 40 units of insulin was needed to control the diabetic syndrome on a diet containing 401 g. of carbohydrate, 102 g. of protein, and 11 g. of fat; but, when insulin was omitted, ketosis rapidly developed and the patient died in typical diabetic coma. It is noteworthy that in such patients susceptibility to overdosage with insulin is well-marked and hypoglycæmic attacks are frequent. It is thus certain that deprivation of insulin will produce diabetes in man, but, as J. P. Peters [51] says: "No condition approaching the gravity of the disorders of metabolism encountered in severe spontaneous human diabetes has been produced in man by destruction or removal of the pancreas."

Precise measurements of insulin sensitivity have not yet been made in the pancreatic diabetes either of man or animals, but the ease with which insulin controls the condition, depresses the blood-sugar, and produces hypoglycæmic symptoms indicates that it is of the sensitive type. In general, diabetics giving the sensitive response to the insulin-glucose test and believed to have insulin deficiency are young, whereas those giving the insensitive response are old. Scott and Fisher [62] estimated the insulin in the pancreases of 14 non-diabetic and 18 diabetic patients who died suddenly. The insulin content for the non-diabetics, at all ages, averaged 1·7 units per g. of pancreas, but in the diabetics, though the general average was 0·4 unit per g., the lower values were in the young, and normal values were found in some of the elderly arteriosclerotic patients. Cori's results on alloxan-diabetes indicate that, in primary insulin deficiency, overfunction of the anterior pituitary gland should occur, but it seems unlikely that this would be more than a normal response to an abnormal condition. It is not therefore surprising that attempts to detect A.P.E.-like factors in the urine of sensitive diabetics have given negative results, even when methods which gave positive results in other types of diabetic were used.[32]

From a pathological standpoint the correlation between islet lesions and human diabetes is disappointing. Lesions similar to those in experiments on animals occur, but, though they are more frequent in diabetic patients, they can also be found in non-diabetics.[70] Morbid histology therefore provides an unsound basis for inference. Nevertheless, since the discovery of alloxan diabetes, the possibility of toxins which act directly on the islet cells cannot be discounted.

ACROMEGALY AND DIABETES

The diabetes associated with acromegaly in its active phase is insensitive in type.[15 32] From the urine of such patients large amounts of an A.P.E.-like factor can be extracted, and this, on injection into animals, produces a state of insensitivity to insulin.[32] Radiotherapy directed to the anterior pituitary gland diminished both insensitivity to insulin and the amount of A.P.E.-like factor in the urine of such patients. Normal rabbits give a sensitive response to the insulin-glucose test, those injected with A.P.E. an insensitive response.[24]

But in acromegalics in whom the disease has burnt out the response may be sensitive. In such a case, with diabetes of 20 years' duration but in which the acromegaly appeared to have been quiescent for 10 years, no A.P.E.-like factors were found in the urine. The sequence is reminiscent of the experimental type of pituitary diabetes. During the period of injections of A.P.E. the dogs are insensitive to insulin; when permanent diabetes have been established, and injections have been stopped, they become sensitive.[75]

Digitized by Google

CUSHING'S SYNDROME AND DIABETES

Diabetes in Cushing's syndrome is insensitive in type and may be conspicuously ameliorated by irradiation of the pituitary gland [30] or, when the syndrome is due to adrenal tumour, by adrenalectomy.[66] Substances which produce insensitivity to insulin on injection into rabbits have been recovered from the urine of such cases.[32] Glycosuria and marked resistance to insulin can be produced in rats by 11-dehydro-17-hydroxy-corticosterone.[35] Injection of adrenocorticotrophic hormone produces, both in rats [36] and men,[6 7] a temporary diabetes which is characterised by insensitivity to insulin.

DIABETES AND DESTRUCTION OF INSULIN

When insulin is injected intravenously it rapidly disappears from the blood-stream, and Mirsky and Broh-Kahn [48] claim to have isolated from the liver an enzyme which destroys insulin. It is evident that, if the rate of insulin destruction were excessive, patients with that abnormality would give an insensitive response to the insulin-glucose test. Such patients, however, have not been discovered. A similar situation would arise if insulin were neutralised by some form of antibody. Such cases are known and have shown resistance to injected insulin [37a]; but there is no evidence that a similar immunity to endogenous insulin exists.

"ORDINARY" DIABETES AND INSULIN SENSITIVITY

The diabetes of acromegaly and of Cushing's syndrome accounts for only a small minority of the total cases of insensitive diabetes, for the majority of elderly diabetics are of this type. Investigation of such cases has not revealed any trace of an insulin inhibitor like A.P.E. in their urines.[32] Originally it was thought that the diabetes in these patients might be an exaggeration of the impaired glucose tolerance which develops in normal people on carbohydrate starvation; and even that the condition might arise as the result of long-continued ingestion of low-carbohydrate diets.[30] No evidence in support of this view has been obtained. But it would be very short-sighted to imagine that all cases of insulin insensitivity must necessarily be due to direct inhibition of insulin. Failure of intracellular carbohydrate metabolism at points farther along the chain, or incapacity to store ingested carbohydrate as glycogen or fat, could equally well give rise to insensitivity. Such possibilities require consideration now.

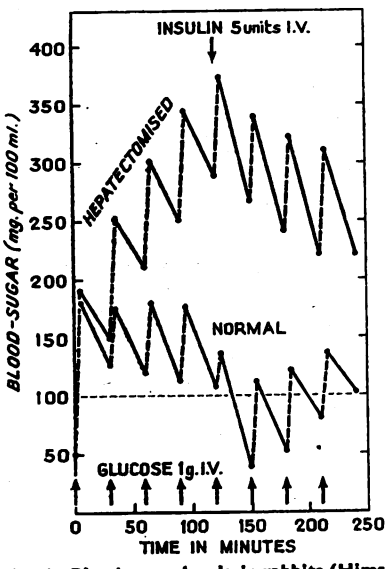


Fig. 4—Blood-sugar levels in rabbits (Himsworth 1935 unpublished), showing that hepatectomy impairs glucose tolerance and action of insulin in suppressing exogenous hyperglycæmia. Hepatectomy two hours before the experiment began. Resting blood-sugar level in normal rabbit 110 mg. per 100 ml., and in hepatectomised rabbits 62 mg. per 100 ml.

LIVER LESIONS AND DIABETES

Hepatectomy, in experiments on animals, impairs sugar tolerance and produces relative insensitivity to insulin (fig. 4). These effects are readily understandable, for the operation has deprived the body of the organ particularly adapted to store a sudden influx of glucose. But to obtain such impairment 80% or more of the liver must be removed, and it is probably because of this immense reserve that diabetes of this type is rare clinically. Occasionally, however, diabetes develops suddenly in patients whose livers are extensively infiltrated with cancer, and at necropsy it is seen that the growth has virtually performed a hepatectomy. Whether a similar diabetic syndrome can arise from functional failure, rather than mechanical curtailment, of hepatic function is uncertain, but experimental evidence indicates that this may happen in the course of infections.

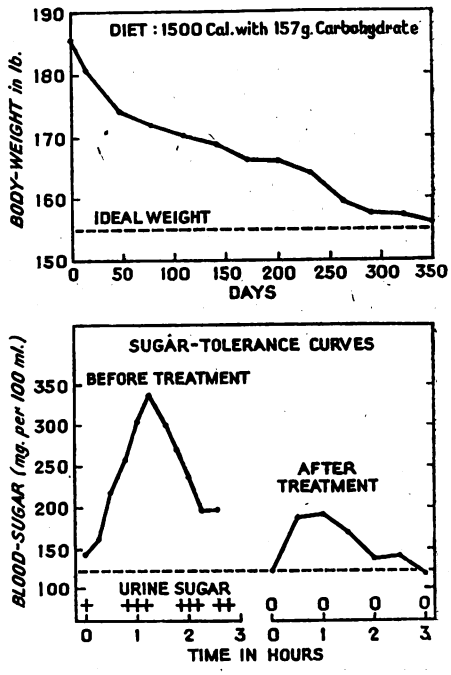


Fig. 5—Body-weight curve of diabetic patient, showing return of glucose tolerance to normal on reduction of weight.

OBESITY AND DIABETES

The association of obesity and diabetes, especially in the elderly, is well recognised, and it is notorious that such patients often live for years, in reasonable health, without any insulin therapy. These cases show many peculiar features.[49] In contrast to the young patient with severe diabetes the ability of these patients to oxidise carbohydrate is apparently unimpaired. Ketosis seldom develops and is light even on starvation. Despite the mildness of the symptoms astonishingly large amounts of insulin may be required to clear the urine of sugar. These patients give an insensitive response to the insulin-glucose test and can tolerate large excess of insulin without developing hypoglycæmic symptoms. But, most striking of all, reducing the patient's weight by any dietary means not only removes the symptoms and signs of diabetes but also restores the sugar-tolerance curve to normal (fig. 5); and this result is all the more remarkable because it is achieved by the very measure—semi-starvation—which impairs carbohydrate tolerance and insulin sensitivity in normal people. In the sense that there is no detectable abnormality of carbohydrate metabolism, as long as obesity is prevented, such cases can be regarded as cured.

It is a commonplace that animals deposit fat when eating only carbohydrate, and that emaciated diabetics replenish their fat depots when given insulin. Recent work throws a new light on these observations, for it has been shown that, in the normal animal, the major portion of the carbohydrate eaten is stored as fat,[41] ten times as much being synthesised into fatty acids as is used to form glycogen.[67] In animals made diabetic with alloxan, however, formation of fatty acids from glucose is practically in abeyance, and the sugar which

Digitized by Google

would normally have been used for this purpose is excreted in the urine.[68]

Three years ago Dr. R. D. Lawrence[39] analysed a remarkable case of lipodystrophy and diabetes, explaining the diabetes as due to failure of insulin to change ingested sugar into stored fat. The patient showed almost complete absence of adipose tissue. Severe lipæmia was a conspicuous feature, and its degree was related to the control of the diabetes, being high when this was poor. It was, however, unaffected by wide variations in the amounts of dietary fat and carbohydrate. Despite the lipæmia ketosis was absent and, on starving, the patient produced no more ketosis than a normal person. Under observation the basal metabolic rate (B.M.R.) rose gradually to + 170%, but after thyroidectomy it fell to + 40%, when myxœdema developed. Large amounts of insulin were required to control hyperglycæmia, but at necropsy the pancreas appeared normal and the glycogen content of the liver and muscles was within normal limits. The response to the insulin-glucose test was insensitive. This remarkable case has many suggestive features. Despite the apparent severity of the diabetes, ketosis, usually the surest indication of a severe diabetic condition, was absent, and the glycogen content of the tissues was normal. There is, in fact, little evidence of failure to metabolise carbohydrate as such. Nor is there evidence of failure to metabolise fat. That the patient could synthesise fat is shown by her maintaining lipæmia on a high-carbohydrate régime; that she could katabolise it is indicated by her developing mild ketosis on starvation. But the point that is incontrovertible is that she had lost the ability to store fat, and this seems sufficient to explain her whole syndrome. It seems that, when large doses of insulin were given, the greater part of the carbohydrate ingested was forced along the direct line of carbohydrate metabolism, little remained to be turned into fat, and consequently lipæmia did not develop. When, however, the only insulin available was a small dose, plus that from the patient's pancreas, little more than the normal amount of carbohydrate went along this line. There remained the large amount which, in a normal person, would have been synthesised into fat and stored as such. Some was so synthesised but, since it could not be stored, accumulated in the blood. In some as yet obscure way this failure to store seems to have halted the synthesis of fat, and as a result the remaining sugar accumulated in the blood and spilled over into the urine. This sustained hyperglycæmia in the presence of normal carbohydrate metabolism might perhaps explain the high B.M.R.

Consider now the obese diabetic who is "cured" by slimming. Is it possible that, in the obese state, the stores of fat are filled to capacity, with the result that the proportion of ingested carbohydrate which is normally turned into fat cannot be disposed of and is excreted as glucose in the urine? Lawrence[39] has suggested that it is, and I fully agree with him. This would explain the observed ability to oxidise carbohydrate as such, the relative good health without insulin therapy, the absence of ketosis, the insensitivity to exogenous insulin, and the beneficial effects of depleting the body's store of fat.

Heredity and Environment in the Ætiology of Diabetes

HEREDITY

The age-incidence curve for human diabetes mellitus has the form shown in fig. 6 and might well be made up of two component curves each representing the incidence of a distinct condition, the first of which was common in the earlier age periods, the second in the later. Recent studies on the heredity of diabetes lend some support to this idea, and it is of interest that insulin-sensitive diabetes is common in the young and insulin-insensitive diabetes in the elderly.

In most diabetic clinics a family history of diabetes is found in about 30% of adult patients, but in children's clinics a familial incidence of 52% has been found. Similarly, if one identical twin develops diabetes the other does so sooner or later; but no such relationship exists between dissimilar twins. On the basis of their data Pincus and White[52,53] suggested that diabetes was transmitted as a mendelian recessive characteristic, but the data of other workers have not proved reconcilable with such a unitary hypothesis. Harris's recent investigation[18] points to a different conclusion. He found a significantly higher rate of cousin marriages among the parents of diabetics who developed the disease before the age of 30 than among the parents of those who developed it later. This, he believes, suggests hereditary differences between cases of late and early onset, and he suggests that the patients with milder diabetes of late onset are heterozygous for the abnormal gene, whereas those with severe diabetes of early onset are homozygous.

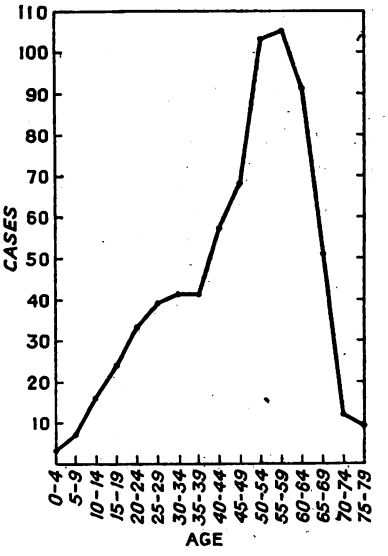


Fig. 6—Age-incidence of onset of diabetic symptoms in 700 consecutive cases of diabetes mellitus seen in hospital practice.

How hereditary factors act is unknown, but there is good evidence that the susceptibility to diabetes varies. Thus there are large variations in the total amount of A.P.E. needed, and the time required, to produce permanent diabetes in different dogs, and about 20% of rats treated with alloxan prove insusceptible.

DIETARY HABITS

When food-supplies are restricted, diabetic mortality falls; and this fall is confined to diabetics over the age of 45. There has been some reluctance to accept such mortality changes as reflecting changes in the incidence of diabetes; but, now that independent data are available for the incidence-rates in different countries, this objection can be discounted.[25] The dietary factor which parallels these changes most closely is the consumption of fat, and this correlation is surprisingly consistent. The falls during the two periods of war-time rationing are so correlated. The rise over the last fifty years in Western countries has been associated with increasing consumption of fat. The actual incidence in different countries is directly related to the content of fat in the national diet. The higher incidence in urban as compared with rural populations and the increasing incidence with financial status are both correlated with the amount of fat consumed. Finally, race is not a decisive factor in the incidence of diabetes. Immigrant races acquire the diabetic incidence-rates of their new country in proportion as they acquire the habits of its people.[20]

The simplest explanation of these data is that predisposition to diabetes, hereditary or constitutional, is widespread, and that it is the pressure of the environ-

Digitized by Google

mental factor of diet which is disclosing its prevalence. At any particular time the population contains an unknown number of susceptibles. As the diet changes to contain progressively more fat, first the most susceptible and later the less susceptible will be affected, with the result that at any particular time the diabetic incidence-rate and the diet reflect each other.[20]

It is also well established that, as dietary carbohydrate is restricted, sugar tolerance and insulin sensitivity diminish; and on this basis Himsworth indicted the proportion of carbohydrate in the diet as the significant dietary factor in respect of diabetic incidence-rates. Himsworth's suggestion seems ill conceived, for he had himself shown previously[19] that it was the absolute amount, and not the proportion, of carbohydrate in the diet that determined the sugar tolerance. Similarly the dietary survery,[26] which he tried to interpret in the same way, seems to indicate nothing more than that untreated diabetics are hungry, though perhaps showing, like Richter's depancreatised rats,[57] a preference for fat.

We are thus left with the paradox that, though the consumption of fat has no deleterious influence on sugar tolerance,[19] and fat diets actually reduce the susceptibility of animals to diabetogenic agents,[17] the incidence of human diabetes is correlated with the amount of fat consumed. But this correlation does not necessarily mean that fat itself is deleterious, for the consumption of fat may merely indicate other, more important, contingent variables. One such is known, and indicates an explanation. In the individual diet, though not necessarily in national food statistics, fat and calories tend to change together. The change in diabetic mortality is confined to the middle-aged and elderly. It is in this group that the obese diabetic, who is "cured" by weight loss, predominates. It is suggested that dietary restrictions, by preventing obesity, permit these patients to die from other causes without developing clinical diabetes.[25]

INFECTION

It is a clinical commonplace that infection exacerbates established diabetes, and that certain types, especially the staphylococcal, may provoke glycosuria and hyperglycæmia even in hitherto apparently healthy people. Investigation of these latter patients reveals that, by every criterion, they are diabetics as long as the infection lasts. After its subsidence some again become, and remain, normal, but others continue permanently as diabetics. The question therefore arises: "Can infection cause permanent diabetes?" All that can be said is that there are grounds for believing that infection may precipitate manifest diabetes in a person so predisposed, but that the case has not been proved for considering that infection may cause diabetes in subjects with no such predisposition.

How infection produces temporary diabetes, or worsens the existing condition, is not precisely known. It certainly increases the insulin requirements. Many hepatic toxins cause an immediate discharge of liver glycogen and thus produce hyperglycæmia. Soskin[65] has shown that such liver damage interferes with the regulatory function of the liver as regards the blood-sugar, with the result that "diabetic" sugar-tolerance curves are found. It is therefore possible that infection may act, in part, something like hepatectomy.

GROWTH AND PREGNANCY

Young[76] has shown that, when puppies are injected daily with amounts of crude pituitary extract greatly in excess of those required to produce diabetes in adult dogs, they respond with an increased growth-rate but either do not develop symptoms of diabetes mellitus or develop it only after several months. When diabetes does appear, growth stops despite continued treatment with A.P.E. Growth-hormone preparations cause retention of nitrogen, and Mirsky[47] has obtained evidence that their effects depend on normally functioning islets of Langerhans. According to Ogilvie[50] the pancreas of the human infant contains more islet tissue in proportion to body-weight than does that of adults, and Langenfeld[38] has shown that more pancreas has to be excised in puppies to produce diabetes than in adult dogs. Strong evidence has been produced by Young[76 77] that the growth hormone and the diabetogenic factor of the anterior pituitary gland are closely related, if not identical, and he therefore inclines to the view that whether the pituitary factor produces growth or diabetes depends on whether or not the islets can increase their function. In this connexion White's observation[71] that many diabetic children are overheight at the onset of their disease is pertinent.

These observations promise to be of further significance in relation to pregnancy in diabetics. Before the insulin era pregnancy was hazardous to both the diabetic mother and her child. Since the introduction of insulin the risk to the mother has become negligible, but the fœtal mortality-rate has persisted almost unchanged. Attempts to explain the high fœtal mortality as due to failure to control the maternal diabetes have now had to be abandoned. But a most suggestive observation has been made by Miller,[45] who found that the birth-weight and neonatal mortality-rate were both significantly increased in the infants of women who later developed diabetes. The accompanying table, constructed from the data of Barns and Morgans,[3] shows clearly that the high fœtal mortality-rate already exists in the prediabetic period. These observations link with the greatly improved results obtained when œstrogens and progesterone are given to pregnant diabetics.[72] This therapy was devised to counteract a hormonal imbalance thought by some to exist in pregnant diabetics and to cause the toxæmia to which diabetics were supposed to be liable. But, as Barns and Morgans point out, the beneficial effects might equally be due to inhibition of anterior pituitary activity by such therapy, and they have suggested that the high fœtal mortality-rate, in both prediabetic and diabetic states, may be due to excessive secretion of the anterior pituitary growth (diabetogenic) factor. It has since been shown that, when pregnant rats are injected with extracts, rich in this factor the fœtal mortality is 100%.[2]

FŒTAL MORTALITY-RATE IN PREDIABETIC PREGNANCIES

Years before onset of diabetes	No. of pregnancies	Percentage fœtal mortality	Average age of mothers at time of pregnancy (years)
0–5	29	34·5	29·8 ± 5·37
6–10	17	23·5	27·0 ± 4·46
11–15	20	10·0	24·9 ± 3·98
16–20	9	0	22·8 ± 2·8

From the data of Barns and Morgans.[3]

These results seem highly significant. Young's work indicates that the production of pituitary diabetes is an "untoward" effect of a physiological factor, and that this effect can be held in abeyance when, as in the young, islet function is strong. The observation on pregnancy shows that potentially deleterious influences are operative, though masked in the prediabetic period. If the suggestion of Barns and Morgans proves correct, presumably in the prediabetic state the islets are meeting the strain of the excessive anterior pituitary activity, and the possibility of a predisposition of certain people to pituitary overfunction and of unusual vulnerability of the islets of Langerhans must be considered.

Digitized by Google

Secondary Effects of Hyperglycæmia

Many years ago Allen [1] demonstrated that partially depancreatised dogs, given a high-carbohydrate diet, became permanently diabetic, but if given a fat diet or semistarved they did not. The development of diabetes was accompanied by hydropic changes in the β cells of the islets in the pancreatic remnant, and this Allen attributed to the effects of sustained hyperglycæmia. These results have been amply confirmed and extended. It has been shown that, if the hyperglycæmia consequent on injection of A.P.E. is prevented by starvation, fat diets, phloridzin, or insulin, permanent diabetes does not develop; but that, if hyperglycæmia is facilitated by liberal allowances of carbohydrate, it does.[17 40] The development of this diabetes is signalled by lesions in the islet cells and the disappearance of insulin from the pancreas. But most significant of all, Dohan and Lukens [12] have shown that, if a pronounced hyperglycæmia is maintained in normal cats by repeated intraperitoneal injection of glucose, degeneration of the islet cells and permanent diabetes may follow. Cats who reacted to this treatment with only a mild hyperglycæmia did not get diabetes, and, further, Lukens has pointed out that those species which do not develop permanent diabetes after injection of pituitary extracts are also those which do not react to A.P.E. by hyperglycæmia.[40] There is, therefore, strong evidence that hyperglycæmia per se can produce a secondary insulin deficiency.

These considerations remind one irresistibly of the work of Wilson and Byrom [73] on the secondary effects of hypertension and how they disentangled the effects of hypertension per se from the manifestations of the many conditions which might cause a high blood-pressure. We may therefore consider what effects such a secondary insulin deficiency would have in a patient whose hyperglycæmia had previously been due to some condition in which, as was suggested in the case of certain obese diabetics, carbohydrate oxidation was unimpaired. Signs of carbohydrate starvation, such as ketosis, would now appear despite the ingestion of adequate dietary carbohydrate. Weight reduction would no longer "cure" the diabetes. Naturally, if the primary condition were one like active acromegaly, which itself interfered with carbohydrate oxidation, the development of a secondary insulin deficiency would not be detectable. It is thus possible to understand why, even if all cases of diabetes are not due to a primary insulin deficiency, all the patients may ultimately die in typical diabetic coma, and similar islet lesions may be found at necropsy.

Syndrome of Diabetes Mellitus and its Causes

It is rarely possible to define a disease precisely, but it is always possible to characterise a syndrome. In medicine definition entails elimination, for a syndrome is usually first glimpsed in a complex condition, associated with secondary syndromes, from which it has to be disentangled until its essential features are clear. The one essential of the syndrome of diabetes mellitus is an elevation of the blood-sugar level above those limits we regard as normal. On this depend glycosuria and, when its degree is sufficient, polyuria and thirst. But none of these dependent manifestations, nor any others in diabetic patients, are peculiar to diabetes mellitus. And the syndrome can arise in the absence of wasting, ketosis, or any evidence of failure to oxidise carbohydrate. Its one essential criterion is abnormal hyperglycæmia.

The causes of abnormal hyperglycæmia fall into two broad groups according to the site of the primary fault: those in which the primary fault is so situated as to impair the direct line of carbohydrate metabolism; and those in which initially there appears to be no such impairment but rather an incapacity to store ingested carbohydrate as fat or glycogen. In the first group are placed primary deficiency of insulin and inhibition of insulin consequent on overfunction of the anterior pituitary gland. In the same group would be placed any interference with the chain of intracellular carbohydrate oxidation—e.g., hyperglycæmia of experimental thiamine deficiency. The second group would include the abnormal hyperglycæmia of those obese diabetics whose syndrome disappears on weight reduction and that which accompanies hepatectomy whether produced surgically or by tumours. It is not yet clear how several abnormal hyperglycæmias are to be classified. That associated with overfunction of the cortex of the suprarenal gland will probably fall into the group due to direct inhibition of insulin. The ultimate significance of the prediabetic state which exists in some pregnant women remains to be seen. The position of the hyperglycæmias due to infection and to various poisons can only be settled by further data. But, irrespective of the location of the primary fault, the abnormal hyperglycæmia common to all can lead to islet damage and secondary insulin deficiency, and so to the supervention, or aggravation, of an impairment to the direct metabolism of carbohydrate by the cells.

All the primary faults, save one, would cause insensitivity to insulin. The exception is deficiency of insulin. The results of the insulin-glucose test show that, whereas the sensitive response is the rule in the younger age-groups, the insensitive response is usually obtained in the middle-aged and elderly. The incidence of diabetes increases rapidly in middle age; the insulin-insensitive type of diabetic is therefore the most common in any representative diabetic population.

It thus appears that we should accustom ourselves to the idea that a primary deficiency of insulin is only one, and then not the commonest, cause of the diabetic syndrome. That is not to say, however, that in the other types of case insulin therapy is irrational. Insulin is our only means of breaking down any excessive inhibition of the process by which glucose enters the metabolic stream. Within the cell we are dealing with a chain of reactions; and, provided the level of any particular enzyme is not reduced below a minimum, increasing the concentration of the incoming substrate may be expected to whip up the rate of turnover. But there are rare cases in which insulin fails. In them the primary fault is presumably of too great a degree to be overborne by insulin. It is only by discovering the nature of such primary faults that we can hope to improve our therapy and, more important, to prevent the diabetic syndrome.

REFERENCES

1. Allen, F. M. (1913) Studies concerning Glycosuria and Diabetes. Boston.
2. Barns, H. H. F., Lindan, O., Morgans, M. E., Swyer, G. I. M. (1948–49) *Proc. Soc. Endocrinol.* (in the press).
3. — Morgans, M. E. (1948) *J. Obstet. Gynæc.* **55**, 449.
4. Bennett, L. L., Roberts, L. M. (1946) *Amer. J. Physiol.* **146**, 502.
5. Burn, J. H., Dale, H. H. (1924–25) *J. Physiol.* **59**, 164.
6. Conn, J. W., Louis, L. H., Wheeler, C. E. (1948) *J. Lab. clin. Med.* **33**, 651.
7. — — Johnston, M. W. (1948) *Proc. 8th ann. Meeting Amer. Diabetic Ass.* cited in *Nutr. Rev.* (1949) **7**, 17.
8. Colowick, S. P., Cori, G. T., Slein, M. W. (1947) *J. biol. Chem.* **168**, 583.
9. Cope, O., Marks, H. P. (1934) *J. Physiol.* **83**, 157.
10. Cori, C. F. (1945–46) *Harvey Lect.* **41**, 253.
11. Darnaud, C. (1946) *Arch. Mal. Appar. dig.* **35**, 489.
12. Dohan, F. C., Lukens, F. D. W. (1947) *Science*, **105**, 183.
13. Drury, D. R. (1925) *Amer. J. Physiol.* **111**, 289.
14. Falta, W. (1936) Die Zuckerkrankheit. Berlin.
15. Flaum, G. (1938) *Endocrinology*, **23**, 630.
16. Gerard, R. W., Schachter, R. J. (1932) *Proc. Soc. exp. Biol., N.Y.* **29**, 525.
17. Haist, R. E., Campbell, J., Best, C. H. (1940) *New Engl. J. Med.* **223**, 607.
18. Harris, H. (1949) *Proc. R. Soc. Med.* (in the press).
19. Himsworth, H. P. (1935) *Clin. Sci.* **2**, 67.
20. — (1935) *Ibid*, p. 117.
21. — (1936) *Lancet*, i, 127.
22. — (1938) *J. Physiol.* **91**, 413.
23. — (1939) *Lancet*, ii, 1, 65, 118, 171.
24. — (1940) *Brit. Med. J.* i, 719.

Continued at foot of next page

Digitized by Google

INJURIES AND DEATH FROM LIGHTNING

M. J. G. LYNCH
M.B. N.U.I., M.R.C.P.
MAJOR R.A.M.C.,
SPECIALIST IN PATHOLOGY

P. H. SHORTHOUSE
B.A. Camb., M.R.C.S.
MAJOR R.A.M.C.

THE nature of lightning and its effects are concisely given in annotations in *The Lancet* (1944, 1946), on which we have freely drawn. The elements of the lightning flash which may produce injury are as follows (Spencer 1932):

(1) The direct effect of the current.
(2) Superheated air or other objects traversed by the current.
(3) The expanded and repelled air.

The effect of the last Spencer speaks of as the "sledge-hammer blow," well known for the characteristic bursting and tearing of clothes and shoes, and for the way in which it may hurl bodies several yards. It also may cause fractures, concussion, and a diversity of other injuries which may be in themselves fatal. Burns may be caused by elements (1) or (2) of the flash.

Spencer classifies lightning burns into 3 types:

(1) *Linear burns*, $^1/_8$–1 in. wide and up to 1 ft. or more long. These rather resemble the stripes caused by scourging. Not infrequently they follow the lines of greatest perspiration—i.e., creases and folds of the skin.

(2) *Filigree or arborescent burns*, also known as keraunographic markings, or Lichtenberg's flowers, since they were for many centuries supposed to be images of the surrounding flora. Critchley (1932) gives many instances of such burns, which Spencer regarded as of bad prognostic import and evidence of a severe stroke. Critchley, however, says that he has seen them in mild cases and that they disappear within twenty-four hours in patients who recover.

(3) *Surface burns*, occurring beneath metallic objects worn or carried on the person struck. These are real burns due to the great heat (which may fuse the metal) generated by the current, whereas types 1 and 2 are not real burns (*Lancet* 1944), though electric discharge and a spark may occur and lead to a true burn. These surface burns have been described and discussed in *The Lancet* (1944).

Severe lightning burns are rare in patients who survive. However, electric burns in general require careful handling because, owing apparently to vasospasm and thrombosis, they may be more extensive than appears at first examination. Nevertheless, even if necrosis and sloughing occur, the resulting scar is usually pliable and smooth owing to the absence of inflammation (*Lancet* 1944).

EFFECTS ON NERVOUS SYSTEM

Jellinek (1932b), Panse (1925), and Critchley (1932, 1934) have made a long study of the effects of lightning and electricity on the central nervous system, which are as follows:

(1) Immediate effects, consisting of shock, unconsciousness, and suspended animation.
(2) Secondary effects, comprising temporary nervous disorders, visual disturbances, burns, and gangrene.
(3) Remote effects, including various rare complications.

Immediate Effects

More often than not a person struck by lightning falls unconscious immediately. A dictum ascribed to Pliny states: "The man who sees the lightning and hears the thunder is not the one who is struck." That this is not strictly true is now well known and has been pointed out by Charcot (1890). Sestier (1866) and he state that such exceptions are commoner with sheet and ball lightning than with the fork type. Critchley (1934) states that loss of consciousness may be due to syncope or to immediate concussion; it may not take place until after some time, and is then due apparently to the development of cerebral œdema. Though unconsciousness usually comes quickly and suddenly, in some cases various subjective experiences may precede its onset—e.g., visual disturbances such as bright lights (cf. "moons" of electrical mechanics) and, not uncommonly, a sensation as of receiving a terrific blow, usually in the region of the head or back of the neck, and probably due to the expanding and propelled air before the stroke of lightning. While unconscious the person usually lies immobile, and there is none of the restlessness, tremor, twitching, or convulsions which are common in unconsciousness due to electric shock (Critchley 1932). Urination and/or ejaculation of semen commonly occur.

Not uncommonly this unconsciousness amounts in seriously struck patients to what Jellinek (1932b) has called "suspended animation," though Critchley (1934) believes that this is really a rare effect. In this condition the victim falls immediately unconscious, circulation and respiration come to a standstill, and the person is to all appearances dead. Urquhart (1927) has shown experimentally that arrest of the heart by electric shock is due to vagal stimulation, and that the vagal centres in the medulla remain refractory for some time after the initial shock. Alexander (1938) believes the cardiac and respiratory arrest to be due to a central medullary effect. He suggests that cardiac fibrillation is probably rare in electric or lightning accidents, but admits it as a possibility. MacMahon (1929) has prevented electrically induced ventricular fibrillation in animals by giving

PROFESSOR HIMSWORTH: REFERENCES—*continued*

25. —] (1949) *Proc. R. Soc. Med.* (in the press).
26. — Marshall, E. M. (1935) *Clin. Sci.* **2**, 95.
27. — Scott, D. B. M. (1938) *J. Physiol.* **91**, 447.
28. — — (1938) *Ibid*, **92**, 183.
29. — Kerr, R. B. (1939) *Clin. Sci.* **4**, 1.
30. — — (1939) *Ibid*, p. 119.
31. — — (1939) *Ibid*, p. 153.
32. — — (1940) *Ibid*, **4**, 287.
33. Himwich, H. E., Nahum, L. H. (1932) *Amer. J. Physiol.* **101**, 446.
34. Houssay, B. A. (1936) *New Engl. J. Med.* **214**, 971.
35. Ingle, D. J., Sheppard, R., Evans, J. S., Kuizenga, M. H. (1945) *Endocrinology*, **37**, 341.
36. — Li, C. H., Evans, H. M. (1946) *Ibid*, **39**, 32.
37. Kerr, S. E., Ghantus, M. (1936) *J. biol. Chem.* **116**, 9.
37a. Klein, S. P. (1948) *Arch. intern. Med.* **81**, 316.
38. Langenfeld, E. (1920) *Acta. med. scand.* **53**, 1.
39. Lawrence, R. D. (1946) *Lancet*, i. 724, 773.
40. Lukens, F. D. W. (1944) *Yale J. Biol. Med.* **16**, 301.
41. Mackay, E. M., Drury, D. R. (1941) *Amer. J. Physiol.* **132**, 661.
42. Mann, F. C. (1938) *Europe med.* p. 32.
43. — Magath, T. B. (1923) *Amer. J. Physiol.* **65**, 403.
44. Marks, H. P. (1936) *J. Physiol.* **87**, 15P.
45. Miller, H. C. (1945) *New Engl. J. Med.* **233**, 376.
46. Minkowski, O., Weintraud, cited by Young, F. G. (1944) *Annu. Rev. Physiol.* **6**, 427.
47. Mirsky, I. A. (1939) *Endocrinology*, **25**, 52.
48. — Broh-Kahn, R. H. (1948) *J. clin. Invest.* **27**, 549.
49. Newburgh, L. H., Conn, J. W., Johnston, M. W., Conn, E. S. (1938) *Trans. Ass. Amer. Phys.* **53**, 245.
50. Ogilvie, R. F. (1937) *Quart. J. Med.* **6**, 287.
51. Peters, J. P., Van Slyke, D. D. (1946) Quantitative Clinical Chemistry Interpretations. 2nd ed., Baltimore; vol. I, p. 297.
52. Pincus, G., White, P. (1933) *Amer. J. med. Sci.* **186**, 1.
53. — — in Joslin, E. P., Root, H. F., White, P., Marble, A. (1940) The Treatment of Diabetes Mellitus. London.
54. Price, W. H., Cori, C. F., Colowick, S. P. (1945) *J. biol. Chem.* **160**, 633.
55. Radoslav, C. S. (1924) *Wien. Arch. klin. Med.* **8**, 395.
56. Reid, E., Smith, R. H., Young, F. G. (1948) *Biochem. J.* **42**, 19P.
57. Richter, C. P. (1942–43) *Harvey Lect.* **38**, 63.
58. Ricketts, H. T., Brunschwig, A., Knowlton, K. (1945) *Proc. Soc. exp. Biol., N.Y.* **58**, 254.
59. — Stare, F. J. (1945) *J. Lab. clin. Med.* **30**, 594.
60. Russell, J. A. (1938) *Physiol. Rev.* **18**, 1.
61. — (1938) *Amer. J. Physiol.* **121**, 755.
62. Scott, D. A., Fisher, A. M. (1938) *J. clin. Invest.* **17**, 725.
63. Scott, E. L., Dotti, L. B. (1932) *Arch. intern. Med.* **50**, 511.
64. Soskin, S., Levine, R. (1937) *Amer. J. Physiol.* **120**, 761.
65. — — (1946) Carbohydrate Metabolism. Chicago.
66. Sprague, R. G., Priestley, J. T., Dockerty, M. B. (1943) *J. clin. Endocrinol.* **3**, 28.
67. Stetten, DeW. jun., Boxer, G. E. (1944) *J. biol. Chem.* **155**, 231.
68. — — (1944) *Ibid*, **156**, 271.
69. Verney, E. B. (1948) *Brit. med. J.* ii, 119.
70. Warren, S. (1938). The Pathology of Diabetes. Philadelphia.
71. White, P., in Joslin, E. P., Root, H. F., White, P., Marble, A. (1940) The Treatment of Diabetes Mellitus. London.
72. — (1945) *J. Amer. med. Ass.* **128**, 181.
73. Wilson, C., Byrom, F. B. (1941) *Quart. J. Med.* **10**, 65.
74. Young, F. G. (1936) *J. Physiol.* **87**, 13P.
75. — (1939) *New Engl. J. Med.* **221**, 635.
76. — (1941) *Brit. med. J.* ii, 897.
77. — (1948) *Lancet*, ii, 955.

Digitized by Google

atropine, and both he and Urquhart (1927) suggest cardiac injection of atropine and adrenaline in cases of suspended animation, but warn against too much of either drug. Alexander (1938) also suggests from the experimental work of Hooker that, if fibrillation is suspected, intracardiac potassium chloride followed by calcium chloride be tried. The effectiveness of electric countershock for ventricular fibrillation has been established experimentally, but it has never been applied to human cases.

Much doubt has been cast on Jellinek's "suspended animation." Critchley (1934) cites Alvensleben (personal communication), one of the leading German authorities on electrical accidents, as being extremely sceptical about alleged resuscitation after half an hour. However, both Jellinek (1932b) and MacLachlan (1930) have reported successful resuscitation of victims of accidental electrocution, with apparently complete cessation of respiration and circulation, when efficient artificial respiration had been applied for 8–12 hours. MacLachlan, in an analysis, reported excellent results with Sharpey-Schäfer's method: 67% recoveries in over 450 cases. He points out, convincingly, the importance of starting artificial respiration as soon as possible. The recovery-rate was 70% when artificial respiration was begun within 3 min. after the shock, but only 58% if 4 min. or more had elapsed before it was started.

The first sign of recovery is laryngeal movement—the "ultimum movens, primum revivens" of Jellinek. When it returns, artificial respiration should cease, though one should always be prepared to start it again if necessary, since Spencer (1932) cites several instances of patients brought round by artificial respiration only to die later through a second cardiac or respiratory failure.

An important part of treatment is lumbar puncture. Jellinek (1932b) has shown the frequency of cerebral œdema in lightning and electric shock, and has established the existence of high pressure in the cerebrospinal fluid of such cases. He has obtained good results with lumbar puncture.

Secondary Effects

When the patient has recovered consciousness, the commonest and most noted abnormality is paraplegia—keraunoparalysis of Charcot (1890). It is noted by the victim immediately consciousness returns. Often it is described as a sensation of "nothing below the waist," or, as in one of our cases, "as if a heavy weight were on the legs." On examination there is found to be a flaccid paralysis of the legs and lower trunk coupled with an objective sensory loss, complete or partial. Within an hour or so sensation gradually begins to return, and tingling and pins-and-needles are often experienced. Both sensation and motor power return to normal within 12–24 hours. Critchley (1934) remarks that the restoration of power and sensation parallel the recovery of the peripheral circulation. During the period of unconsciousness and for some time afterwards the limbs are cold, blanched or livid, and the toes blue. This severe autonomic stimulation is the most generally accepted cause of the keraunoparalysis. Critchley draws an analogy between it and the hypoæsthesia seen in the Raynaud phenomenon. He says he could not trace any case in which a thorough neurological examination had been carried out during the stage of flaccid paralysis.

Many other secondary effects of a trophic nature and of autonomic origin may be seen in cases of lightning or electric shock (Critchley 1934): "electrical œdema" is fairly common; and cyanosis, pallor, and peripheral arterial spasm of the limbs may be seen. Transient autonomic disturbances in the eye are not rare—e.g., pupillary abnormalities, Horner's syndrome, and papill-œdema. Mydriasis, anisocoria, loss of light-reflex, and pupillary mytonia have been recorded as permanent changes. Alopecia and canities, transient tachycardia, hyperhydrosis, and a peculiar hard œdema of the muscles are described. Not uncommonly there is, on recovery of consciousness, conjunctivitis with intense photophobia. Other recorded abnormalities are detachment of the retina, transient ocular palsies, cataract, and optic atrophy.

Retrograde amnesia is common. Many curious psychological states are described as occurring on or after recovery of consciousness. Charcot (1890) described what he called "the delirium of the man struck by lightning": pallor, trembling, disorientation of thought and confusion of speech, repetitiveness, and emotional lability. Critchley (1934) describes a sensation of prolongation of time, restlessness, irritability, noisy excitement, and anxiety. He also notes that sleep on the night or nights following the accident is usually poor. Panse (1925) described a strange calm and lack of interest in several cases. However, excitement and anxiety rather than tranquility and composure are the rule.

Painful tonic cramps of the muscles of the limbs and trunk have been described by Jellinek (1932b), Critchley (1932), Spencer (1932), and many others. Charcot (1890) described his patient as being unable to drink for some hours after the stroke. Jellinek remarks that laryngismus and trismus may be very severe and can jeopardise artificial respiration. Spencer describes the effect of such cramps as seen in the position of the cadaver—e.g., the body may be found with cup held to mouth, still in the eating position, &c. Jellinek believes that the laryngismus and trismus are neural in origin.

Next in frequency of occurrence to the flaccid paraplegia are hysterical manifestations of diverse forms. Charcot (1890) gave a dramatic description of hysterical hemiplegia and hemianæsthesia, coupled with hysterical loss of taste and smell on the affected side, and concentric constriction of the visual fields. Hysterical deafness, blindness, aphonia, amnesia, fugues, and paralyses of various types are well recognised. Critchley (1932) describes the reappearance of transient dysæsthesiæ in the legs of a lightning case at every subsequent thunderstorm (psycho-recidives).

Remote Effects

Neurological sequelæ are rare. Critchley (1934) has classified them into (1) cerebral, (2) spinal, (3) mixed cerebrospinal, and (4) peripheral nerve lesions, isolated or multiple. He states that hemiplegia and aphasia have been recorded, but that they are usually associated with pre-existing arteriosclerosis. Choreo-athetosis and myoclonus are also recorded. Panse (1925) has described spinal atrophic paralysis which, clinically, is not unlike progressive muscular atrophy. Weeks or months after the stroke wasting develops, accompanied by fibrillation but without sensory disturbances, usually in the muscles supplied by C4–C6. The weakness and atrophy may be unilateral or asymmetrically bilateral. Spasticity gradually develops in the lower limbs. Sphincteric disturbances are usually absent (Leys 1942). Loewenstein and Mendel (1932) described mixed clinical types resembling disseminated sclerosis or general paralysis. These they called electrotraumatic encephalomyeloses. Permanent peripheral neuritic changes, spastic paraplegias, disturbances of sensation, and nerve deafness have been recorded. Critchley (1934) emphasises the importance of distinguishing the neurological effects of lightning from true organic neurological diseases apparently precipitated by the shock, and from organic nervous disorders caused by factors in the accident other than the current—e.g., falls. He, Alexander (1938), Panse (1925), and Jellinek (1932b), emphasise that arteriosclerosis is a predisposing factor in the development of central nervous disease

Digitized by Google

following lightning and electric shocks. Further, both Panse and Jellinek give evidence that arteriosclerosis may develop through repeated minor electrical injuries. Panse has expressed his opinion that the late central nervous disorders may be due to a vascular disease (chronic progressive vasopathy of Marburg).

Many curious effects have been attributed to lightning and electric shock. Psychoses of various types have been attributed to it. Jellinek (1932b) gave one of the first hints of the beneficial effect of electric shock when he described the case of a schizophrenic who was much improved after receiving a shock from a high-tension cable. Critchley (1932) cites the case in which a scirrhous carcinoma of the breast was cured when struck by lightning.

PRESENT CASES

On the afternoon of April 19, 1948, a soccer match was in progress between two Army teams. It was not raining at the time, but a thunderstorm was in the neighbourhood. Suddenly a great fork of lightning struck the pitch in the midst of a group of players. Those in the vicinity were instantly struck to the ground. The rest of the players fell down as if in unconscious sympathy. After a few seconds most of them got slowly to their feet, but some four or five remained motionless on the ground.

One of us (P. H. S.), being in attendance and on duty at the match, went at once to the stricken players. Two men were obviously dead; they were pulseless and livid, their conjunctivæ suffused, and the pupils in the cadaveric position. Both had ejaculated semen. These two, aged 28 years and 18 years 10 months, had been marking each other very closely, being within some 6 in. of each other.

Another casualty was the referee, a man aged 42, who was standing about 10 yards away from the deceased. He afterwards said he did not see the flash, and that he remembered being prostrate on the ground with no feeling in his legs or right arm, all of which were "useless." He had experienced a sensation of being suspended in the air by the neck. He did not lose consciousness. On examination on the football field he was shocked, being cold and clammy, with dilated pupils and a rapid pulse of poor volume. His right arm and both legs were in a state of flaccid paralysis. From his hips downwards he felt "as if a heavy weight were on him." This paralysis gradually disappeared; four hours later he was able to use his right arm. The return of sensation preceded the recovery of motor power. Sensation and use of his legs returned within sixteen hours, though he could not get out of bed until next day. Physical signs in this patient detected on the day after the accident were two "burns" at the base of the toes of the right foot, and one on the medioplantar aspect of the left foot. The burns were small and of the size which might be caused by a cigarette. The upper limbs were normal and, apart from a diminution in power, the lower limbs were normal.

A third player, standing about 5 yards from the two deceased, felt as if he had been hit on the head. He fell and then tried to rise and walk, but he again felt as if he were being hit on the head, and he fell once more and lost consciousness. On return of consciousness after some 2 min. he could not speak. When eventually he did speak his natural stammer was accentuated, and he described himself as "sticking" on a word. On examination he was shocked, cold, clammy, and sweating; his pupils were dilated and his pulse rapid and poor in volume. He revived quickly, however, and within half an hour he could speak, his colour was returning, and his pulse improved. His general improvement continued apace and he was quite fit by the same evening, though he felt "shaken."

It is regretted that the survivors were not further examined but the hours immediately after the accident were devoted to the attempted resuscitation of the two deceased. Artificial respiration (method of Sharpey-Schäfer) was instituted within 2 min. of the accident and carried out by trained personnel for 40 min. 'Coramine' was injected intracardially in both cases, and one was placed in the Drinker apparatus after 40 min. of artificial respiration, but there was no sign of recovery.

Many of the spectators were "affected," but no definite history of unconsciousness could be elicited, and no abnormal physical signs were detected.

The two casualties who recovered did not see the flash though very near—one within 5 yards and the other within 10 yards. Apart from the "burns" on the feet of the referee, no signs of injury to, or burning of, either skin or clothes could be discovered in these two cases, and no visual disturbances, deafness, or hallucinations were described by them.

Necropsies

Necropsy was done on body A 6 hours after death and on body B 18 hours after death. Both bodies were those of well-developed athletic men with no excess fat. There was singeing of the hair over the left frontotemporal region, left abdomen, and all the pubis of body A, and of the hair on the right frontotemporal region, right chest, abdomen, pubis, and right lower limb of body B. Body A had numerous small subcutaneous hæmorrhages in the left circumorbital region, in the superior region of which the hæmorrhages were confluent. On the nasal and inferior portions they tended to be discrete and irregular in shape, and some were present in the skin of the left side of the nose. Body B had a similar ecchymosis in the right circumorbital region, more marked infra-medially, and extending as petechiæ on to the upper right side of the nose. On the right sclera and cornea of body A, extending horizontally across both from the outer margin of the pupil to the lacrimal caruncle, there was an area of superficial erythema and denudation of epithelium 2 mm. broad. An exactly similar condition was present on the left sclera and cornea of body B. Distinct cutaneous arborescent marks (fig. 1) were present on the necks and chests of both bodies. These marks were confluent in the necks and spreading out into distinct fronds over the clavicles and upper chest. In body A this was mostly on the left side; in body B it predominated on the right side of the neck and upper chest. In both bodies similar though smaller marks were present in the skin over the upper medial third of the anterior aspect of the left thigh, corresponding to the natural position of the glans penis. Over both internal malleoli of body B there were small punctate puncture-like marks. Otherwise the skin of both bodies appeared normal, apart from intense cyanosis; this was shown in the nails as an intense slate-blue.

Fig. 1—Aborescent cutaneous marks on neck and chest after death from lightning.

Internally, in both bodies, the great veins were considerably engorged. There were moderate extravasations of blood in the regions of the lower thirds of the sternomastoid muscles in both bodies. In body B there was a small amount (about 3 ml.) of gelatinous blood and mucus in the larynx above the vocal cords, and there was a moderate amount of fluid blood in the trachea and bronchi. In the lower lobe of the right lung of body A there were three superficial hæmorrhages. The left lung showed no hæmorrhages, but in the upper lobe, running in a curved direction (convexity lateral) from 1 in. lateral to the apex of the lobe down to its medial margin, were two bands of pleural and subpleural dark-reddish brown discoloration, about 1 cm. in width and 2·5 cm. apart. In body B there was a large wedge-shaped thrombosed hæmorrhage in the anterior aspect of the upper lobe of the left lung and $1^1/_2$ in. below the apex. There was also a small area of subpleural hæmorrhage in the anterior interlobular surface of the lower lobe of the left lung. On the superior aspect of the posterior surface of the lower lobe of the right lung of body B there was a diffuse area of superficial hæmorrhage $2 \times 1^1/_2$ in. and about $^1/_2$ in. deep. In both bodies there was considerable generalised congestion of the lungs.

Digitized by Google

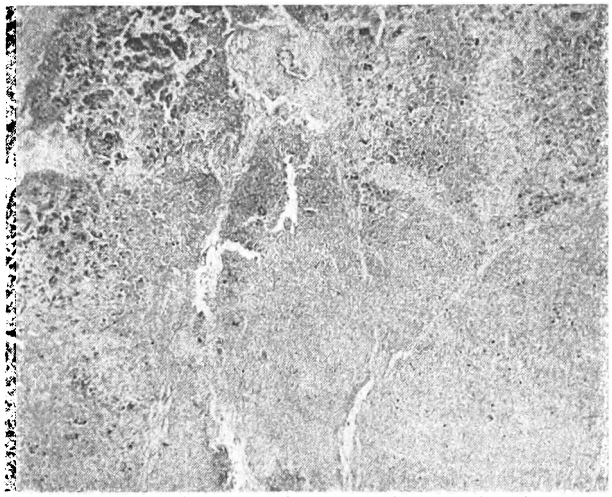


Fig. 2—Necrosis of pancreas. (Hæmatoxylin and eosin.) (× 42.)

In body A there were some twenty petechiæ on the posterior aspect of the epicardium, especially on the right side. Otherwise the heart was entirely normal. In body B there was a large solitary "milk spot" on the infundibular portion of the epicardium, and the mitral valve showed old inactive rheumatic endocarditis of mild degree. In both bodies the spleens were greatly congested and enlarged, being twice the normal size.

In the right paracolic gutter of body B there was an area of retroperitoneal bleeding extending downwards and medially, with an irregular linear tear in the overlying peritoneum.

In both bodies there was diffuse hæmorrhage into the caudal two-thirds of the pancreas. There was an intense dark discoloration of the organs in these areas but no evidence of fat necrosis. The hæmorrhage too was confined to the pancreas.

The livers, suprarenal glands, and kidneys appeared normal, apart from considerable congestion.

Both brains showed scanty minute hæmorrhages. These were just visible, and were seen to advantage in the floors of the fourth ventricles and in the region of the hypothalamus. No obvious œdema or other abnormality could be determined at necropsy.

The blood of both cadavers, apart from the hæmorrhages described above, showed no sign of clotting.

Histological Examination

In both bodies the lungs were extremely congested. In the hæmorrhagic areas the alveolar walls and the walls of the small blood-vessels and the capillaries were ruptured in numerous places, and there was widespread and diffuse intra-alveolar hæmorrhage. Especially where the hæmorrhages were densest, much of the extravasated blood appeared to have been hæmolysed or fused into a hyaline eosinophilic mass, in some areas of which red-cell ghosts were seen. In no area did the extravasated blood appear to have been due to diapedesis of erythrocytes, and there was no evidence of wandering of histiocytes, which Alexander (1938) suggested.

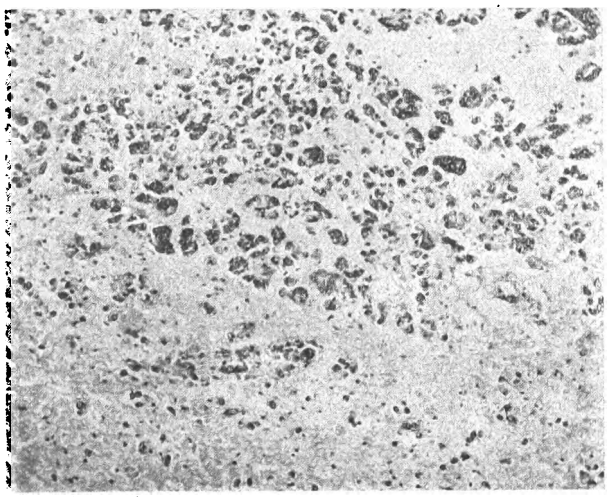


Fig. 3—Incomplete necrosis of pancreas. (Hæmatoxylin and eosin.) (× 104.)

The pleural markings found at necropsy showed histologically as extreme capillary congestion and interstitial hæmorrhages in the pleura and subpleural area of lung to a depth of some 300–500 μ.

In both bodies the liver showed no abnormality apart from widening of the sinusoids and moderate acute passive congestion. Renal congestion was well marked in both. The erythrocytes in most of the glomerular tufts were fused into an eosinophilic hyaline mass. There was pronounced granularity and swelling of the cells of the proximal convoluted tubules.

There were microscopic hæmorrhages in the tissue surrounding the suprarenal glands, which were extremely congested, especially in the zona reticularis and medulla.

No histological abnormality was found in the myocardium with the routine stains used (hæmatoxylin and eosin and Van Gieson) nor with Heidenhain's method.

In the pancreas of each case there was massive lobular and multilobular necrosis (figs. 2, 3, and 4), with diffuse hæmorrhage mostly in the interlobular areas but also in many of the necrotic lobules. Necrosis was not patchy but rather massive. At the margins of the necrosed areas, where normal

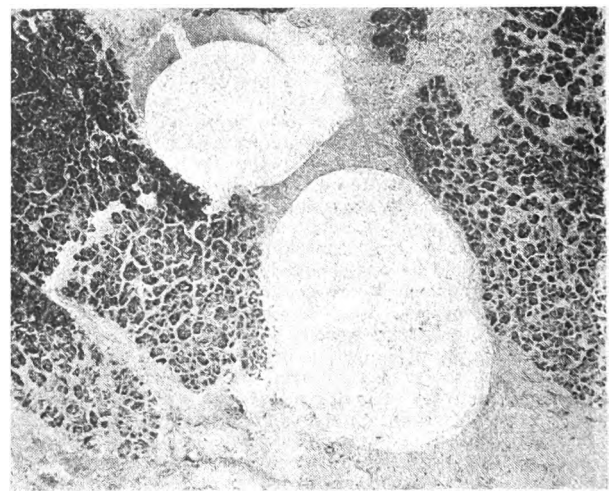


Fig. 4—Pancreas showing two large gas-bubbles in a hæmorrhagic interlobular region in an area of relatively mild necrosis. (Hæmatoxylin and eosin.) (× 39.)

tissue began, the margins of the relatively normal lobuli displayed, to a varying depth, a similar but milder necrosis, gradually decreasing as it merged into the normal tissue. In the areas of greatest necrosis the cells were not recognisable; in the less severely affected regions the cells were just discernible as shrunken homogeneous finely granular or hyalinised eosinophilic bodies, often showing somewhat swollen and deeply staining nucleoli, which appeared to have survived better than the cell bodies. The erythrocytes of the hæmorrhages tended strongly to fuse into a solid mass of eosinophilic hyaline coagulum. The walls of some of the veins in the interlobular tissue were ruptured. A few clear circular cyst-like spaces were seen in the hæmorrhagic areas, as if containing gas (fig. 4); the largest measured about 1000 μ. Shrunken cells of the parenchyma often produced an appearance of a honeycomb of clear spaces. In addition to the ruptured blood-vessel walls already described, in many areas all the layers of the vessel walls, especially the endothelium, appeared swollen and distrupted and, in places, also partly hyaline and necrotic, as if subjected to the same necrosis seen in the parenchyma. Vessels were unrecognisable in the grossly necrotic areas.

The brain tissues, after being fixed in formol-saline, were stained routinely with hæmatoxylin and eosin, and with Giemsa for Nissl degeneration. Significant findings were hæmorrhages, ranging in size from 2 or 3 mm. to microscopic perivascular extravasations, in the floors of the fourth

Digitized by Google

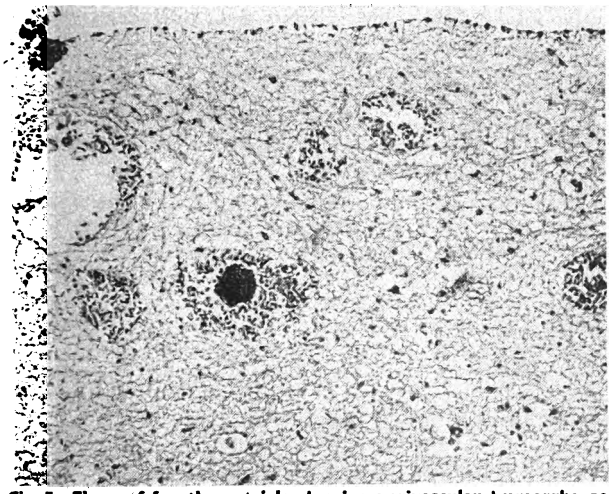


Fig. 5—Floor of fourth ventricle showing perivascular hæmorrhages and distension by gas. (Hæmatoxylin and eosin.) (× 140.)

ventricles (fig. 5) and in the suprachiasmatic regions. Sparse microscopic hæmorrhages were also found in the pons, left corpus striatum, subependymal thalamus, and mid-brain. There were no macroscopic hæmorrhages in the cortex, and microscopic perivascular hæmorrhages were very sparse here also. Congestion was severe throughout both brains, and early red thrombi, some fused and hyaline, were seen in sections from many regions.

In some areas of perivascular hæmorrhage, and round some of the vessels showing red thrombi, there were clear empty spaces, which appeared too large to have been caused by shrinkage during fixation. Also, in a few of these, the brain tissue surrounding the spaces appeared compressed, and in some the cells appeared injured and partly degenerate.

DISCUSSION

In the lungs of lightning and electric-shock deaths Jellinek (1932b) has described congestion and œdema as a characteristic finding. Alexander (1938) has described pulmonary œdema, congestion, and diapedetic hæmorrhages in electric-shock fatalities. In our cases no evidence of œdema was found, and hæmorrhages, where present, were large and certainly not due to diapedesis.

In the skeletal and cardiac muscles Jellinek (1932a) has described a peculiar spiral malformation of the fibres, and he has produced these experimentally in guinea-pigs. He states that the change is best seen in sections stained by Heidenhain's method. He likens the appearance of the affected fibres to a screw bolt, the fibre appearing to have a dense spiral thread wound round its circumference at an angle of 45° to the long axis. Also, the intervening segments of the myofibril are pulled out of alignment so that the normal longitudinal striations lie at right angles to the spiral. He interprets his finding as a pattern produced by the electrodynamics.

We have been unable to find any reference to pancreatic necrosis caused by lightning or electricity. In our cases the necrosis was most marked in the tails, being widespread in this region. The heads of the pancreas in both cases appeared normal. Though hæmorrhage was very well marked and diffuse it was not an essential part of the necrosis. Many completely necrotic lobules showed no hæmorrhage. Also the necrosis had a coagulative appearance, and this, together with the occasional "gas spaces," appears to indicate that heat played at least some part in the process. The only lesion somewhat similar to this which we have been able to find in the published reports is that described by Pietrusky (1926), who found hæmorrhage and colliquative necrosis in the myocardium of a patient killed by a 220 V. direct current. What part, if any, post-mortem autolysis played in the pancreatic necrosis is difficult to assess. However, at necropsy the gross appearances of the pancreas in both bodies were similar, the caudal two-thirds being intensely discoloured and obviously hæmorrhagic (necropsy of body A was done six hours after the accident). The necrotic process may be parallel or akin to Jellinek's (1932b) gross *elektrische Immediatnekrosen*.

It is in the brain, however, that the most vital histopathological changes have been sought, and found with varying success, by many workers. Congestion of the brain is accepted by all. Jellinek (1932b) has done pioneer work in demonstrating the frequency and importance of cerebral œdema. His findings are now universally accepted. Critchley (1934) states that, with very severe injury as from direct hits from lightning or in experimental electrocution with high-tension currents, the entire brain and parts of the cord may be swollen, softened, and even diffluent. Innumerable instances of cerebral œdema have been published—e.g., Panse (1925), Alexander (1938), and Dickson (1947). However, in our cases cerebral œdema was evident neither macroscopically nor microscopically.

Large vascular tears in the cerebrum or cord have been described by Critchley (1932), Dickson (1947), and others. They usually occur when the cranium is directly struck by lightning or, as in Dickson's case, when the electric shock is received directly by the brain tissue. Petechial and perivascular hæmorrhages are accepted as typical findings. Jellinek (1932b) has described destruction of the blood-vessel walls, endothelial swelling of the capillaries, and thromboses. The latter findings were present, though sparse, in the brain in our cases. Kawamura (1921) first observed homogenisation of the blood in the small blood-vessels of the brain and other organs. Pietrusky (1926) also found this curious change. It was notable in most organs in our cases, and was seen in the extravasated blood in the lungs and pancreas. Other investigators have found hæmoglobinuria and blood-pigment casts in the renal tubules. Alexander (1938) discusses this phenomenon and argues that it is due not to any specific electrical effect on blood but to the fact, as Jellinek (1932b) believes, that death takes place much later than is assumed. Alexander and Newbill (cited in Alexander 1938) have shown experimentally that thrombi require at least 30 min., and perivascular foci of disintegration with incomplete necrosis and demyelination required 2 or 3 hours, to develop after local cessation of cerebral circulation.

Jellinek (1932b), Jaffé (1928), Spitzka and Radasch (1912) and Alexander (1938) have described, in electrical death, dilations of the perivascular spaces measuring 25–250 μ in diameter. These were sometimes bridged by fine strands of neural connective tissue. The spaces were surrounded by an area of compressed nervous tissue. Spitzka and Radasch believed these to be caused by electrolytic liberation of gas; Jaffé considered they were due to heat. Certainly, in legal electrocution cases, Werner (1923) recorded cerebral temperatures up to 145°F. However, this finding cannot be applied to other electrical deaths without reservation, because in legal electrical execution the current passes through the brain for a relatively long time. Others, including Dickson (1947) have described interstitial spaces in the brain. Dickson found that they were larger and more numerous in the grey than in the white matter. His explanation of their preponderance in the grey matter is that the liquid content of the grey (83–85%) is greater than that of the white matter (70%).

The interpretation of changes in the Nissl substance in electrical or other injuries is extremely difficult. Langworthy (1930) states that delay of only a few hours in performing a necropsy may cause a considerable

Digitized by Google

tigrolysis. For this reason many of the reports of chromatolysis are valueless. Again, the interpretation of morphological findings in the Nissl substance is difficult for two further reasons:

(1) The type and appearance of the granules vary in the different nerve-cells. In general, somatic motor cells have large granules throughout the cytoplasm; autonomic cells show large granules round the edges only; and sensory nerve cells display widespread dust-like fine granules.

(2) The fixative used is important. Hopkins (1924) has shown that the size and degree of definition of the Nissl granules varies greatly according to the fixative used. Mixtures of 95% alcohol and 10% formalin in equal parts or 10% formalin containing 2–5% acetic acid, or Zenker's fluid containing 2–10% acetic acid, give the best results. Formalin alone was used by us.

In our cases importance was attached to Nissl-body findings only in body A, because necropsy of body B was delayed for 18 hours. The stain used was dilute alkaline Giemsa with differentiation in absolute alcohol and colophonium. Various degrees of tigrolysis were found in the cerebellum, olivary bodies, suprachiasmatic region, caudate nucleus, and orbital cortex. The striking feature was the extreme patchiness of the change. Small groups of cells showed Nissl degeneration, with or without eccentricity of the nucleus, vacuolation of the cytoplasm, and haziness or bursting of the cell margin, whereas cells only 100–200 μ away appeared perfectly normal. There was no spatial pattern of degeneration. Many investigators, including Langworthy (1930), have observed this extreme patchiness of cell degeneration.

Of the cause or causes of the changes seen at necropsy in the brain in deaths from lightning or electric shock Critchley (1934) says: "Probably the blood-vessels constitute the main routes for the passages of currents through the brain, and many of the changes found at autopsy are explicable on the basis of a primary vascular lesion." Certainly the changes are not in themselves specific for electrical death. Critchley says that changes due to current, to heat caused by it, and to toxæmia after burns or cerebral concussion would be difficult of differentiation one from the other. Langworthy (1930) states: "The abnormalities following the electric injury are characteristic for injured nerve-cells no matter what the inciting cause." Pietrusky (1926) considered most of the findings consistent with "internal suffocation." Lieut.-Colonel Albert Sachs has told us that his findings in the brains of heat-stroke victims have been broadly similar to ours.

SUMMARY

Two cases of fatal lightning stroke, together with temporary effects in two others, are described. The outstanding features of the fatal cases were hæmorrhages and necrosis in the pancreas and keraunographic marks on the exterior of the body.

Our thanks are due to Colonel J. A. Crawford, officer commanding Cambridge Hospital, Aldershot, for permission to publish these cases; Lieut.-Colonel Albert Sachs, R.A.M.C., A.D.P. Southern Command, for helpful advice and criticism, especially in connexion with the staining of the Nissl substance; Captain J. Sugden, R.A.M.C., for the photograph of the skin markings; and Mr. J. Napper, of the Welsh National School of Medicine, for the photomicrographs.

REFERENCES

Alexander, L. (1938) *J. industr. Hyg.* **20**, 191.
Charcot, J. M. (1890) *Wien. med. Wschr.* **40**, 9, 57, 104.
Critchley, M. (1932) *Brist. med. chir. J.* **49**, 285.
— (1934) *Lancet*, i, 68.
Dickson, W. E. (1947) *J. Path. Bact.* **59**, 3, 359.
Hopkins, A. E. (1924) *Anat. Rec.* **28**, 157.
Jaffé, R. H. (1928) *Arch. Path.* **5**, 837.
Jellinek, S. (1932a) *Wien. klin. Wschr.* **45**, 37.
— (1932b) Electrische Verletzungen. Leipzig.
Kawamura (1921) *Virchows Arch.* **231**, 570.
Lancet (1944) ii, 446.
Lancet (1946) i, 351.

Continued at foot of next column

TUBERCULOUS ABSCESS AT THE SITE OF PENICILLIN INJECTIONS

G. B. FORBES, M.B. Aberd.
ASSISTANT PATHOLOGIST

F. G. St. CLAIR STRANGE, F.R.C.S.
ORTHOPÆDIC SURGEON

KENT AND CANTERBURY HOSPITAL

THE formation of an intramuscular tuberculous abscess subsequent to, and at the site of, injection of penicillin has been reported previously. The case of Ebrill and Elek [1] was that of a boy with a staphylococcal axillary abscess for which penicillin was given by intramuscular injection into both thighs. He was readmitted to hospital three months later with an abscess of the left thigh which proved on bacteriological examination to be tuberculous. Hindenach's [2] case was that of a small boy with tuberculous abscesses of both thighs following the injection of penicillin in those sites, the primary lesion for which penicillin was given being a cervical abscess.

We believe that this unfortunate complication of penicillin therapy is not so rare as the paucity of published reports suggests. We have recently seen another case, and we know of two more. We therefore wish to urge a more complete bacteriological investigation of "sterile" pus from penicillin-treated patients.

CASE-RECORD

A male cashier, aged 29, was admitted to hospital on Dec. 10, 1947, with a history of pyæmic arthritis of the right hip-joint at the age of 15. He had been more or less continuously under treatment since that time, and had had local symptoms in the right ulna (1943) and the right third metacarpal (1934 and 1940), which had, however, both subsided without operation in two or three weeks. Details of these incidents are not known, but it is thought that they may have been low-grade pyæmic phenomena.

On the present occasion he had pain in the right buttock, and an acute abscess was found there. The hip was clinically and radiologically ankylosed in fair position, with 4 in. of combined shortening. Since the abscess was deeply situated, the patient was given systemic penicillin, of which he received 10·5 mega units, involving some 42 injections into the lateral aspect of the left thigh, over a period of three weeks. The abscess subsided without sinus formation, and the patient was discharged on Jan. 6, 1948. He was seen again as an outpatient two weeks after his discharge and was allowed to return to work.

On Feb. 2, 1948, he attended the outpatient clinic with three days' history of a swelling in the left leg. A diffuse swelling was found on the outer side of the middle of the left thigh; this was soft, fluctuant, and fairly tender, but not red. There was no tenderness in the inguinal lymph-nodes on this side, which were mobile and only just palpable.

The patient was readmitted on Feb. 23, and the abscess, which had formed at the site of the penicillin injections, was aspirated. The pus contained acid-fast bacilli morphologically typical of tubercle bacilli, and a heavy pure growth of *M. tuberculosis* (human) was obtained on Lowenstein-Jensen medium. Routine culture on ordinary media gave no growth. A guineapig inoculated with the pus died of generalised abdominal tuberculosis five weeks after the injection. A Mantoux test was done only after the development of the abscess, and, as might be expected, was strongly positive. The erythrocyte-sedimentation rate at this stage was 20 mm.

1. Ebrill, D., Elek, S. D. *Lancet*, 1946, ii, 379.
2. Hindenach, J. C. R. *Proc. R. Soc. Med.* 1947, **40**, 161.

MAJOR LYNCH, MAJOR SHORTHOUSE: REFERENCES—*cont.*

Langworthy, O. R. (1930) *Bull. Johns Hopk. Hosp.* **47**, 11.
Leys, D. (1942) *Edinb. med. J.* **49**, 657.
Loewenstein, K., Mendel, K. (1932) *Dtsch. Z. Nervenheilk.* **125**, 211.
MacLachlan, W. (1930) *J. industr. Hyg.* **12**, 291.
MacMahon, H. E. (1929) *Amer. J. Path.* **5**, 333.
Panse, F. (1925) *Mschr. Psych. Neurol.* **59**, 323.
Pietrusky, F. (1926) *Dtsch. Z. ges. gerichtl. Med.* **6**, 535.
Sestier, A. D. F. (1866) De la foudre. Paris.
Spencer, H. A. (1932) Lightning, Lightning-stroke and its Treatment. London.
Spitzka, E. A., Radasch, H. E. (1912) *Amer. J. med. Sci.* **144**, 341.
Urquhart, R. W. I. (1927) *J. industr. Hyg.* **9**, 140.
Werner, A. H. (1923) *N.Y. med. J.* **118**, 498.

Digitized by Google

in 1 hour (Wintrobe). There was no clinical or radiological evidence of tuberculosis in chest or abdomen; gastric lavage and examination of fæces for tubercle bacilli proved negative.

A small sinus developed at one of the punctures, but this healed within two weeks, and the patient was again discharged on May 8. Five months later there was no recurrence of discharge and no evidence of an abscess, though there was still a little residual thickening at the site.

DISCUSSION

This patient's case-report before we first saw him in December, 1947, is incomplete, but the available evidence points to a primary diagnosis of acute osteomyelitis of the upper end of the right femur at the age of 15, with spread to the right hip-joint, producing a septic arthritis. A series of local exacerbations and metastatic abscesses then followed, and latterly responded well to penicillin therapy without the need for surgical intervention. Though bacteriological proof is lacking, it seems probable that the causal micro-organism was a penicillin-sensitive staphylococcus. The clinical and radiological findings and the course of the disease are much more in keeping with a chronic staphylococcal infection than with a tuberculous one, though it is impossible to be certain that the original hip lesion was not tuberculous. The postpenicillin abscess was, so far as we can ascertain, the first and only manifestation of tuberculosis.

Ebrill and Elek [1] contended that the abscess in their case was a primary tuberculous one, probably due to the introduction of virulent tubercle bacilli with the penicillin solution. They based this view on the elimination of other possible sources of infection. They emphasised the absence of any evidence of tuberculosis in their patient other than the postpenicillin abscess. We too have been unable to detect a focus of tuberculosis elsewhere in the body of our patient, but we none the less favour Hounslow's [3] view that such abscesses are most likely to be postprimary—i.e., occurring in a person already the subject of tuberculosis and harbouring a cryptic primary focus. The primary lesion may be in a part of the body where its detection is difficult—e.g., the alimentary tract—or, if it is in a more accessible position, the primary lesion may be so minute as to escape detection though still capable of causing a transient bacillæmia. Devitalised tissues, or a small hæmatoma at the site of penicillin injection, would act as a favourable soil for the lodgement and multiplication of tubercle bacilli carried by the blood-stream, a course of events similar to that believed to occur in tuberculosis of bones and joints following injury. The fact that the abscesses in Hindenach's case were situated in both thighs further supports the hæmatogenous theory.

The possibility of infection by direct inoculation of tubercle bacilli, either in the penicillin solution or in the apparatus used to inject it, is unlikely but cannot be entirely dismissed. It is the practice in this hospital (as in most) to inject penicillin with syringes reserved solely for this purpose; the use of penicillin syringes for aspiration is strictly forbidden. At the same time there may be a tendency among nurses and sisters to exercise less than usual care in the sterilisation and handling of penicillin syringes in the mistaken belief that penicillin is a potent universal antiseptic. For this reason we endorse the plea of Ebrill and Elek for a more rigid aseptic technique in the administration of penicillin, even though we believe that the condition described here is usually the result of a hæmatogenous infection.

SUMMARY

A case of tuberculous abscess developing deeply in the thigh at the site of previous penicillin injections is described. Reasons are given for supposing that the infection was hæmatogenous.

3. Hounslow, A. G. *Lancet*, 1946, ii, 617.

LONG-ACTING PREPARATION OF TESTOSTERONE

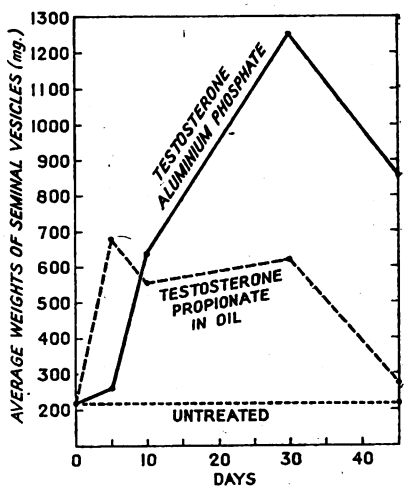
E. CARLINFANTI F. D'ALÒ L. CUTOLO

From the Istituto Sieroterapico Italiano, Naples

THE therapeutic efficiency of hormones is much influenced by the route and form of administration. High concentrations in the blood and tissues are sometimes necessary, and these are most easily attained by using the intravenous route. In our laboratories a water-soluble derivative of testosterone has been synthesised which is well tolerated when injected intravenously, even in large amounts, and has given satisfactory results in certain morbid conditions, such as polycystic mastitis.

On the other hand, for the protracted maintenance of a physiologically useful concentration in the blood repeated inoculations are impracticable; and means had therefore to be found for effecting continuous slow absorption from the site of injection. The maximum of utilisation is not easily attained, since excessive concentrations in the blood are rapidly corrected by renal excretion and by destruction in the liver.

This type of problem has been partially solved in the field of insulin therapy, but no easy solution has been found to date in the use of synthetic hormones. One method of overcoming the difficulty is the subcutaneous implantation of compressed pellets from which the hormones are slowly absorbed. This method has two serious disadvantages: surgical operation is involved, and intolerance of the drug by the tissues often leads to imperfect healing and expulsion of the pellet. Efforts have therefore been made to find alternative means of obtaining the desired depot effect with a less radical procedure. The usual aqueous suspensions of the hormone are unsuitable because they are composed of crystals of various sizes, the largest of which can be injected only through a coarse needle.



The use of insoluble aluminium salts as adjuvants in vaccine prophylactics suggested to us a way of preparing testosterone which has a very protracted action, can be administered with ordinary fine needles, and causes no untoward reactions. This new preparation also has the advantage that it is always ready for use and remains stable for a long time. We are convinced that the same method could be applied equally successfully to other hormones, both synthetic and natural.

PREPARATION

To a solution of 1 g. of crystalline testosterone (melting-point 154·5°C) in 10 ml. of 96% ethyl alcohol is slowly added, with constant stirring, 20 ml. of an aqueous suspension of aluminium phosphate 7 mg. per ml. The mixture is allowed to sediment, and the supernatant fluid is decanted off. The residue is made up to 40 ml. with saline solution.

In this work we used pure testosterone and not the propionate ester, since the former is less irritant.

Digitized by Google

AVERAGE WEIGHTS OF SEMINAL VESICLES OF CASTRATED GUINEAPIGS AFTER ONE INJECTION OF TESTOSTERONE 0·25 MG. PER G. OF BODY-WEIGHT

Time after injection (days)	Testosterone propionate		Testosterone aluminium phosphate	
	No. of guineapigs	Average weight of seminal vesicles (mg.)	No. of guineapigs	Average weight of seminal vesicles (mg.)
3	2	683	2	262
7–8	7	566	4	638
30	4	620	4	1255
45	6	277	2	859

In 24 guineapigs the average weight of the seminal vesicles was 218 mg.

Aluminium phosphate as used by Holt[1] in the preparation of his diphtheria prophylactic (P.T.A.P.) was adopted by us because of its easy preparation and desired properties.

Experiments have been made on guineapigs, which, like rats, show atrophy of prostate, seminal vesicles, &c., after castration. We have taken advantage of the regenerating effect of the hormone on the atrophic vesicles resulting from castration. This regeneration rapidly regresses after the disappearance of the hormone from the body. In preliminary experiments we have observed that twenty days after castration the seminal vesicles of a 400 g. guineapig weigh on an average 218 mg. (24 guineapigs examined). Twenty days after castration a group of guineapigs were given a subcutaneous inoculation of 25 mg. per 100 g. of body-weight of testosterone propionate dissolved in oil, and another group received the same amount of pure testosterone adsorbed on to aluminium phosphate, administered in the same way. The effects of the two preparations on the weight of the seminal vesicles (see table and figure) show that one inoculation of the ester-in-oil leads to a rapid rise and fall in vesicle weight, whereas the new preparation produces a greater and longer-continued action, reaching a peak not earlier than thirty days after administration.

SUMMARY

A preparation of testosterone with depot action is described. It is stable and can be administered with a fine needle. It has the advantage of reducing the frequency of injections to one a month or less and obviates the need for surgical implantation of pellets.

A WHEEL-CHAIR

A. G. BRUCE POOLE
M.B. Edin.

THE wheel-chair described here has been built for a man with major disablement following infantile paralysis. No originality is claimed, but the special features it embodies may be of interest.

The chair has been made to fit a tall young man wearing a Forrester-Brown brace and callipers. His disablement amounts to a total loss of function of the muscles of both legs and of the right arm, with subtotal loss of function of those of the left upper arm and of the lower abdomen. He cannot walk, raise himself to the sitting position, move his body, or lift his left hand to his mouth; but he can use his left forearm and hand. The problem has been to design a chair in which he can remain all day for every purpose, even when travelling in a motor-car—i.e., a chair in which he can be self-supporting wherever he goes. At night a plaster shell is used.

In its evolution there have been three models, each built of a different material: wood, steel, and aluminium. Wood was cumbersome. Steel was satisfactory. The model in steel was in use for about six years; but it had some disadvantages compared with the present aluminium model (fig. 1).

The materials were as follows:

Material	*Description*	*Outside dimensions (in.)*	*Parts*
Aluminium	Channel	1·0 × 0·8125 × 0·0625	Frames
	Tube	0·048 × 0·648 and × 0·75	Supports and handle-bars
	Sheet	0·36 × 24 × 36	Coverings
		0·64 × 24 × 24	Gusset-plates and hinges
		0·125 × 24 × 24	
		0·25 × 24 × 24	
	Rod	Assorted	Nuts, &c.
	Rivets	1/8 diam. × 7/16 & 3/8	..
Steel	Sheet	1/16 & 1/8	Runners, &c.
	Tube		Back supports
	Bolts, &c.	Assorted	..
	Ball-races	..	..
Tin	Sheet	1/16	Hinge-lining
Wood	..	..	Block inserts
Leather or canvas	..	..	Linings

The aluminium is an alloy used in aircraft construction. Channel—i.e., U-shaped material—was selected for the framework, because it is easier to join and to support

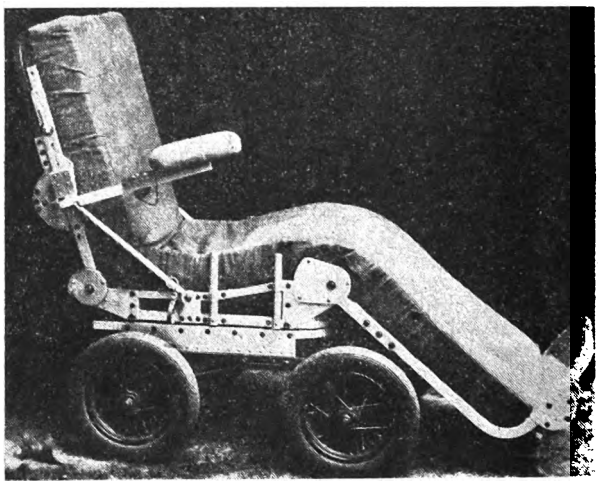


Fig. 1—The aluminium chair.

than tubing and is not particularly difficult to shape by bending. Apart from an adequately appointed workshop the only special pieces of apparatus required were bending-machines, which were made in the workshop.

The foundations of the chair proper consist of three frames—back, seat, and leg—each constructed of channel bent to the required shape and joined at one place only by plate and rivets. The seat frame is linked to the back and leg frames by hinges which work on the principle of those used on hinged callipers. The hinges were specially designed, and each set varies slightly according to the requirements of the chair. They all contain stops to limit the movement at the required range and are lined with tin to prevent the aluminium from dragging. All the moving parts are fitted with ball-races to give ease of movement and to prevent wear. Each part was made separately as a unit, and the chair was assembled with bolts to allow of any unit being removed, should replacement be necessary. Without upholstery and fittings the chair consists of two main parts: the chassis with its wheels, and the chair proper.

THE WHEEL-CHASSIS

The chassis is made up of three separate parts: (1) axles, springs, and supporting structure of steel made

1. Holt, L. B. *Lancet*, 1947, 1, 282.

Digitized by Google

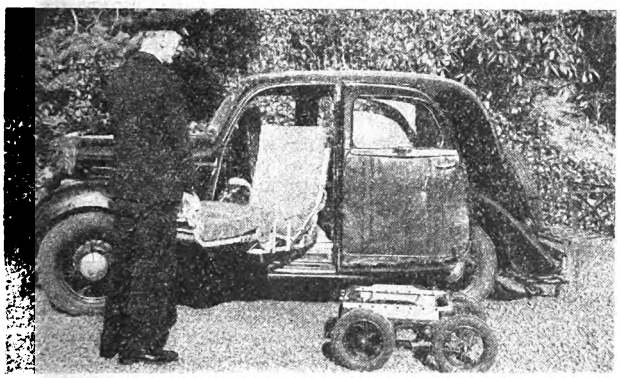


Fig. 2—Transporting the chair.

from a cut down Richards chair; (2) Dunlop pneumatic 12 × 2 in. cycle-type wheels with ball-bearings as used on light barrows; and (3) a special aluminium and steel fitting designed for attachment of the chair. This special fitting consists essentially of runners with guides, grips, and fasteners, and is so placed over the axles that the chair is balanced when the back is up or down.

The chair is simply and rapidly attached. The base of the chair, on which are four small wheels, is placed on the runners, and as the chair is pushed home it is guided automatically into channel pieces that grip the front and rear transverse bars of the base. Once in position the chair is fixed by fasteners placed at the back of this fitting. The chair and wheel-chassis can then be lifted off the ground and the whole carried as one unit.

For travelling by car the wheel-chassis is detached and placed on the luggage grid, and the chair is accommodated on the floor of the car (fig. 2). A 10 H.P. saloon car with four doors is sufficiently commodious to take the chair after one of the front bucket-seats and the back seat have been removed. One passenger can still be carried in the back. As a refinement a floor-board is fitted.

THE CHAIR PROPER

Though the assembled chair proper may appear complicated, the back, seat, hinges, and the leg-rest are simple in design and construction.

The back consists of a single frame to which are bolted gusset-plates to hold a fixed handle-bar and to house the hinges of a movable one. The fixed bar for lifting is made of tube. The movable one for pushing is made of channel blocked with wood and covered with leather to make it pleasant to handle. The back is attached to the seat hinges and held in position by supports which work on the principle of one tube sliding within another, fixation in the desired position being effected by pin and slot. When the chair is pushed forward or pulled back, the main thrust is taken through these supports. In the sitting position they hold up the back at 25° from the vertical, but when the back is let down they are not in action, the back in this position being supported on the stops in the hinges. Thus, to lower the back, all that is necessary is to pull out the pins.

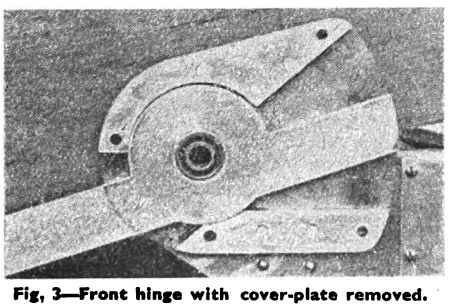


Fig. 3—Front hinge with cover-plate removed.

The seat in its initial stages of construction consists of a single frame; on this uprights are bolted which support an upper frame bent to conform roughly to the anatomical shape of the buttocks. Attachment of the front and rear hinges completes the seat piece as a unit.

The hinges are an important part of the chair. Each consists of two main parts: fixed, and movable. The fixed part is made of $^1/_8$ in. sheet and is bolted to the side of the seat frames and, because the corners are rounded, it is also bolted to the transverse portions of the frames; this is done by means of a plate rivetted at right-angles to the hinge. Such a method is an advantage in that it prevents sideplay. To give the rear hinges additional stability a transverse bar is fitted which also acts as an additional handle-bar for lifting. The movable part is made of $^1/_4$ in. sheet, a cover-plate enclosing it. The front hinge with its cover-plate removed to display the internal workings is shown in fig. 3.

The leg-rest consists of a single frame reinforced with cross-members, covered with thin sheet aluminium, and fitted with a handle-bar for lifting.

UPHOLSTERY AND FITTINGS

Leather is used to line the back and seat, though canvas is also satisfactory. Attachment is by lacing rather than stitching, so that tension can readily be adjusted. Any material is inclined to sag and to squeeze the buttocks and thighs. To prevent this happening, a bar of wood is placed transversely across the material to maintain the necessary tension in the required place. A Dunlop honeycombed rubber mattress measuring 6 ft. × 18 in. × 4 in. and weighing 15 lb. covers the back, seat, and leg-rest. In addition, small wedge-shaped rubber cushions are used to support the feet and to wedge them gently when they are in position.

Fig. 4—Table in use in low position.

The fittings are as follows:

(1) A head-rest, consisting of a light metal frame covered with canvas, is used when the back is down. For attachment it is fitted with prongs which slip into slots on the chair.

(2) A hinged splint is attached to the brace to support the left arm.

(3) An arm-rest, fitted to the chair to support the right arm, can be raised or lowered and swung round to the rear to be out of the way, and bears a pad sliding in a slotted groove to support the wrist and hand.

(4) A table has been specially designed, since the disabled person sits up leaning slightly back and cannot raise the left hand to the mouth unless the upper arm is supported. The height of the table and its proximity to the body are adjusted for writing or for meals by using a set of legs of the required length. The legs are of wood and are supported by metal tubes attached to the chair and fitting into slots under the table. The top is the width of the chair and has three leaves each of a different length linked by hinges so that the table can fold and fit closely to the body when used either in the low or the high position (fig. 4)

(5) A stand to hold a musical instrument, and another to hold music.

Digitized by Google

Before his disablement the young man played the clarinet. Loss of function of the right hand deprived him of this hobby; but as soon as he realised what could be achieved by aids he determined to try to play an instrument which requires the left hand only, and selected the French horn. A stand with many joints was then designed to hold and adjust it. He is now in demand by local amateur orchestras.

Being self-contained in his chair he is, for practical purposes, able to lead the life of an ordinary citizen. He has graduated at a university and has now taken his place in business.

DISCUSSION

The chair was designed from several years' experience in the daily use of a previous model in steel.

The main considerations were that the chair should be comfortable, easy to manipulate, easy to transport, and self-contained. Where there is wasting of muscles over an extensive area, pressure must be borne evenly over the whole of the affected parts. For this reason the seat, back, and leg-rest were designed, when covered with a honeycombed rubber mattress 4 in. thick, to conform roughly to the anatomical shape of the body, a fine degree of adjustment being possible by altering the tension of the lacing. Provided all wrinkles are removed from the clothing when the disabled person is placed in the chair, comfort is not disturbed when the back is lowered for change of position. The urinal is used with the back lowered; the bedpan with it raised. To place the bedpan in position, the technique is to lower the back, raise the buttocks, slip the bedpan into position, then raise the back, and cover the thighs with a carbon-impregnated cloth. Two attendants are required, though one can manage.

For ease of manipulation all the moving parts are fitted with ball-races. Without ball-races the moving parts soon wear out. Once wear sets in, with the amount of man-handling the chair is subjected to, the construction loses its stability. Ball-races are therefore not a refinement but essential. The design of the hinges and their method of fixation make the chair rigid, though there is some whip in the material. The chair weighs 31 lb.

Ease of transport has been achieved by designing a detachable wheel-chassis with a simple attaching device. There is no difficulty in loading the chair into a car, any passer-by in the street can be called on to give a hand. The wheel-chassis weighs 39 lb. The weight could be reduced slightly by fitting solid rubber tyres to the wheels; but the pneumatic-tyred wheels, though heavier, are a great boon, especially for cross-country work, and make the chair look as if it had been built for a disabled person rather than an invalid.

The chair is self-contained as regards fittings, such as writing-table, dining-table, head-rest, and arm-rest. These fittings are easy to carry and thus make it possible for the disabled person to take his place in society.

This chair has passed through its users' trials successfully and is giving satisfactory results. The cost of its construction is difficult to estimate, because it was not made in a commercial workshop, and each part was cut from raw material and shaped by hand. It took a long time to make, but its usefulness is an adequate reward for the time spent. The materials are not costly. In this article technical details have been purposely omitted, but I will be pleased to give them to anyone who may wish to construct a chair on similar lines.

I wish to thank my father, Major-General L. T. Poole, C.B., D.S.O., M.C., for his guidance, and Mr. B. N. H. Thornley, of the developments department of the Northern Aluminium Co. Ltd., for selecting the materials required.

Medical Societies

EDINBURGH OBSTETRICAL SOCIETY

Incoördinate Uterine Action

AT a meeting of this society on Feb. 9, with Dr. E. C. FAHMY, the president, in the chair, a paper on incoordinate uterine action in labour was presented by Prof. T. N. A. JEFFCOATE (Liverpool).

Professor Jeffcoate criticised the use of the term "uterine inertia" on the score that incoördinate uterine action was often associated with high muscle-tone, especially in the middle and lower zones, or with spasmodic violent contractions, or with a constriction ring. The clinical picture was one of prolonged labour with slow dilatation of the cervix, despite the presence of strong uterine contractions and the absence of gross disproportion. Pain, which was unusually distressing, was felt predominantly in the back; sometimes, when it assumed a down-bearing nature before full dilatation of the cervix, it appeared to arise through spasm of the lower bowel. All degrees of incoördinate action might be found; and it was particularly liable to occur in the presence of disproportion.

Of 101 cases observed in Liverpool, 62 were seen in private practice and 39 in hospital. The incidence in hospital cases was 0·6%; the condition was seen more often in private practice, but it was not possible to work out any very reliable figures of its incidence here. The disorder was almost entirely confined to primigravid patients, but the ætiological influence of advancing age had been exaggerated. Premature rupture of the membranes did not appear to be a direct cause, since this occurred in only 22 cases, whereas in 56 the disordered action of the uterus was recognised prior to rupture. Indeed, even when the membranes were unruptured the uterine disturbance was sometimes enough to cause embarrassment of the fœtus. The significance of the occipitoposterior position as a cause of incoördinate action had been confirmed, and delayed engagement of the head in occipito-anterior position was noted often.

The maternal and fœtal dangers of this condition had diminished with the introduction of chemotherapy, better general care of the parturient, caution over anæsthesia, and readiness to resort to cæsarean section late in labour. Nevertheless, the dangers were still present, although in the two series no mothers died and the fœtal loss by stillbirth and neonatal death was only 12%. Professor Jeffcoate estimated that but for cæsarean section the fœtal mortality would have been in the neighbourhood of 50%.

A further series of cases had been investigated in respect of remote prognosis. Of 140 severe but non-fatal cases requiring cæsarean section or forceps delivery during the years 1936–46, 91 had been traced. As a result of their experiences more than one-third of these patients decided to avoid further pregnancy; only half had further children. As regards this voluntary infertility, there was little difference between the cæsarean-section group and that in which forceps had been used; but all the women who had lost their first children tried subsequently to conceive, while contraception was practised only by those who had a living child. A few women embarked on further pregnancy only when promised that delivery would be by elective cæsarean section. In general terms the follow-up showed that in a large proportion of cases the behaviour of the uterus was much more efficient in the second labour, and that whereas cæsarean section might be necessary in the first labour there was a good chance of vaginal delivery in the second. The ease of the second delivery appeared to be to some extent proportional to the stage of dilatation reached by the cervix at the first labour. When full dilatation had been attained, even if the baby had been delivered dead and with difficulty, the second labour was usually easy. Caution was therefore necessary in advising elective cæsarean section solely because of a "bad obstetric history."

In the control of disordered uterine action, the administration of analgesics and antispasmodics, particularly morphine and pethidine, remained the chief line of attack. Professor Jeffcoate reported generally dis-

Digitized by Google

appointing results with intravenous magnesium sulphate, trinitroglycerin, and œstrogens. After intravenous administration of dilute solutions of oxytocin in glucose-saline, as recently advocated by Theobald and others, two of his patients had suffered most severe pain without any change in the nature of the contractions, which remained incoördinate. In each of 11 cases tetraethyl-ammonium chloride had appeared to produce a strong and sustained uterine contraction, sufficient in 1 case to cause alarm for the fœtus. When this contraction had passed off, the patients experienced more frequent, and apparently stronger, uterine contractions for up to one hour; but again there was no evidence of alteration in the nature of the contractions, and 2 cases of constriction ring persisted.

Professor Jeffcoate criticised the contention that fear and emotional tension were important in the ætiology of incoördinate uterine action; for this condition did not recur in deliveries after the first, even when the first had been sufficient to daunt the stoutest heart. He thought that an unnatural resistance of the soft tissues of the lower part of the uterus might be more important than neuromuscularim balance resulting from fear. In conclusion he classified inefficient uterine action under the headings of (1) inertia proper, (2) incoördinate uterine action, and (3) cervical dystocia.

Reviews of Books

Critical Studies in Neurology

F. M. R. WALSHE, M.D., F.R.C.P., F.R.S., physician to University College Hospital and to the National Hospital for Nervous Diseases, Queen Square. Edinburgh: E. & S. Livingstone. 1948. Pp. 256. 15*s*.

OF late years research in medicine has come to be regarded as almost synonymous with the discovery of new facts. As Dr. Walshe points out in the foreword of this book, the climate of opinion does not favour the critical. The facts, however, need interpretation, and, if this is not consciously sought, an erroneous interpretation is often unconsciously assumed. Thus the distinction between critical and creative research is an artificial one, as was well shown by the work of Hughlings Jackson, in whose discoveries it is impossible to separate the rôle of reflection from that of observation. Hence, in his new book Dr. Walshe is employing the Jacksonian method. All but one of these essays have previously been published in *Brain*, but it is to be hoped that, gathered thus into one volume, they will reach a larger public. The first, on the anatomy and physiology of cutaneous sensibility, contains a criticism of the views of Head and Rivers and an account of recent work chiefly on the peripheral organisation of sensation. This is followed by a study of the motor cortex and the pyramidal tract, in which Dr. Walshe discusses the attempt to delimit the motor cortex in terms of its cellular structure and reasserts his objection to Fulton's view that there is a functional difference between area 4 and area 6. The third essay, on the mode of representation of movements in the motor cortex, is a study of the inferences which can be drawn from Jacksonian convulsions concerning the functional organisation of the motor cortex. Dr. Walshe believes that movements are represented not by a mosaic of isolable points but "on a plan of wide and overlapping fields, each of which has a focus wherein the movements of a given motile part are mainly, but not exclusively, localised." Then follow two shorter papers in which the same theme is developed, and the last chapter is on the integration of medicine and is a discussion of those philosophical principles which have found a practical expression in the rest of the book. Differentiation and integration in the development and activities of the organism are paralleled by observation and interpretation in the sphere of the mind. These are the systole and diastole of medical research—the opposites without which, as Blake says, there is no progression. This is Dr. Walshe's salutary message for our times, and here he is both preacher and practitioner.

Detailed Atlas of the Head and Neck

RAYMOND C. TRUEX, M.S., PH.D., associate professor of anatomy, College of Physicians and Surgeons, Columbia University, New York; CARL E. KELLNER, artist in the department of anatomy of the college. New York and London: Oxford University Press. 1948. Pp. 162. 75*s*.

THE most valuable atlases of anatomy have usually resulted from the coöperation of anatomists and artists. Such an association of Professor Truex with the artist Carl E. Kellner has been fully justified by the production of this accurate and attractive atlas of the anatomy of the head and neck. All the drawings in the first part of the book are from original dissections, and are notable for their clearness and their exact portrayal of successive stages in the dissection of particular regions. Outstanding features are the representation of the anatomy of the junctional regions of the neck with arm and thorax, and the instructive approaches to the dissection of various other regions (such as that through the middle cranial fossa and petrous temporal bone into the infra-temporal region). The second section contains some excellent drawings of skeletal structures. Finally, a series of coronal and transverse sections display in fine detail the topographical relations of structures in the neck and cranium. The large size of most of the drawings, together with a judicious use of colour for vessels, nerves, and (in the skull) separate bones and muscle attachments, make the various structures pleasingly distinct and favour the rapid comprehension of relationships. This atlas will be welcomed by teachers; it will also be of real value to the student for reference, and to the surgeon who wishes to review quickly the approach to cervical or cranial structures.

Anæsthesia for the Poor Risk

W. W. MUSHIN, M.B., D.A., director, department of anæsthetics, Welsh National School of Medicine, Cardiff. Oxford: Blackwell Scientific Publications. 1948. Pp. 65. 7*s*. 6*d*.

THIS is an excellent little book. Lightly written, it allows the reader to survey a wide range of anæsthetics pleasantly in one evening by the fireside. These one-page essays, the first of which gives its name to the book, teach nothing of technique, but much of philosophy, and even more of common sense. It could more helpfully have been entitled "The Intelligent Doctor's Guide to Anæsthetics"; and every surgeon would be the better for reading it.

Tuberculosis

A Discussion of Phthisisgenesis, Immunology, Pathologic Physiology, Diagnosis, and Treatment. FRANCIS MARION POTTENGER, A.M., M.D., LL.D., F.A.C.P., emeritus professor of medicine, University of Southern California; director of the Pottenger Sanatorium and Clinic for Diseases of the Chest. London: Henry Kimpton. 1948. Pp. 597. 60*s*.

THE key to Dr. Pottenger's book is his confession that fifty years of medical practice have left him with very little phthisiophobia. He looks on tuberculosis as a disease which is only mildly infectious and which offers the greatest possible opportunity for eradication. The primary infection is to him a vaccination, and, were it not for the fact that it sometimes provides a focus from which future metastases arise, it would be a desirable form of immunisation. With these basic conceptions in his mind and long practical experience to draw on, he sets out to portray tuberculosis as a sometimes destructive but more often a localising and healing disease with a hopeful prognosis. In fact he has a sturdy faith in the resistance of the patient, in the great value of the good sanatorium, and in the skill and guidance of a wise physician—sometimes reinforced by a surgeon. In all this the book is essentially clinical in its outlook, with the emphasis on the good vintage of the ancient régime.

There are separate chapters on each of the classical methods of examination—inspection, palpation, percussion, and auscultation—and only the same allowance (and a short one at that) for radiology. In discussing the search for the tubercle bacillus, Dr. Pottenger rightly emphasises the value of concentration methods of examining sputum; but newer methods such as gastric lavage and laryngeal swab cultivation are not stressed. Morbid anatomy receives less attention

Digitized by Google

perhaps than it deserves as a background of the disease, though there are useful chapters on the primary complex and reinfection and a valuable series of no less than five on complications. The triad of open air, rest, and a well-selected diet is fully honoured, and pulmonary tuberculosis in childhood, so often relegated to an insignificant section in textbooks, receives due attention. New ground is broken in two chapters on the visceral neurology of tuberculosis in which he discusses the action of various reflexes in phthisis. Dr. Pottenger believes that tuberculin therapy plays an important part in treatment—after using it for half a century he has seen only the happiest results—and he expands his views to the length of a whole chapter; but he gives little notice to modern chemotherapy.

He takes his stand indeed on the diagnostic and therapeutic methods which have well and truly stood the test of his long experience; but he leaves the reader wondering whether, in these days of extreme specialisation, a general textbook on pulmonary tuberculosis can really be based on the experience of a single writer.

The Modern Management of Gastric and Duodenal Ulcer

Editor: F. CROXON DELLER, M.D. Edinburgh: E. & S. Livingstone. 1948. Pp. 227. 20s.

Dr. Deller has presented a well-balanced description and review of the treatment of gastric cases. It is refreshing to follow his broad approach to the management of the patient as well as to the management of his local disease. Diagnosis from the clinical aspect is well considered and there is a good chapter on radiology with careful description and discussion of the variations in the appearances of gastric lesions. The chapter on the Decision on Treatment is particularly good, and the detailed instructions for treatment will be useful to the general practitioner in his everyday work. Perhaps too much of the book is given over to minute description and illustration of technical points in surgical operations on the stomach, which are fully covered by other works. Instead, more attention might have been given to modern gastroscopy and the wide bearing it has on diagnosis and choice of treatment. But these are minor criticisms of a well-written and useful work.

Review of Plastic and Reconstructive Surgery

EARL CALVIN PADGETT, M.D., professor of clinical surgery, University of Kansas; KATHRYN LYLE STEPHENSON, M.D., instructor in plastic surgery, Tulane University, Louisiana. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 945. 126s.

THIS is probably the most ambitious work on the surgery of repair yet attempted. The senior author—well known for his invention of the dermatome, or calibrated skin-cutting machine—has tried to unite in one volume principles and practice of repair in all tissues of the body. His untimely death in 1948, before the manuscript was completed, left Dr. Stephenson with a heavy responsibility which she has ably fulfilled.

It is hard to write a comprehensive work on plastic surgery which will satisfy plastic surgeons on the one hand and general surgeons on the other: hence this is a notable achievement. The general principles of repair are covered, and the transplantation of all tissues of the body fully considered. The excellent chapters on trauma include one on burns to which the senior author contributed much during his lifetime. Congenital and acquired defects are fully dealt with, and the reconstructive surgery of special regions and conditions is then discussed in great detail, methods being illustrated by good clear line or wash drawings. Some of the photographs of results are not up to standard and should be replaced. Much work generally regarded as belonging to other fields (thoracic, gastric, orthopædic) might with advantage have been omitted: chapter XIX is almost entirely concerned with operations better presented in many standard orthopædic textbooks, and the same criticism holds for the sections on œsophago-gastrostomy and so-called plastic operations on the kidney pelvis. No doubt this could be remedied in the future editions through which this book is certainly destined to pass.

Teach Yourself Physiology (London: English Universities Press. 1948. Pp. 207. 4s. 6d.).—Mr. David Le Vay, F.R.C.S., gives us a good presentation of physiology at an elementary level along conventional lines. It is brief, businesslike, and attractively illustrated, and designed as a useful rather than an inspiring introduction. It can be recommended to those who have practical facilities, or whose work provides them with experience of the human body.

Thomson-Walker's Genito-Urinary Surgery (3rd ed. London: Cassell. 1948. Pp. 956. 60s.).—Mr. Kenneth Walker has undertaken an onerous task in bringing up to date this old favourite. He has certainly succeeded in preserving the personal character of the book, perhaps at the expense of retaining material which must now be considered obsolescent. The fact that a third edition of the work has been called for is evidence of its popularity.

Refraction of the Eye (3rd ed. London: Henry Kimpton. 1948. Pp. 287. 27s. 6d.).—There have been no radical changes in this American book. Indeed it is not easy to find points of difference from the previous edition. Prof. Alfred Cowan describes in detail the properties of lenses and mirrors and the optical properties of the eye, the methods of prescribing glasses from the plane mirror to the ophthalmometer, the testing of muscle balance, and the uses of contact and telescopic lenses. The exposition is clear and concise, and the advice on spectacle-wearing is sound.

Introduction to Public Health (Bristol: John Wright & Sons. 1949. Pp. 271. 15s.).—Dr. E. W. Caryl Thomas's little volume is suitable for junior medical students, health visitors, and others working in public-health departments. It is too elementary to be of service to medical graduates who think of entering the public-health service, though they will find interest in the first two chapters. The chapter on communicable diseases contains little outside the curriculum of a pass examination in general medicine, and one or two statements—especially about the salmonellæ—are open to question. We could have wished that the chapter on National Health Insurance had been replaced by one on the National Health Service Act.

A Shetland Parish Doctor (Lerwick: T. & J. Manson. 1948. Pp. 136. 10s. 6d.).—Dr. H. P. Taylor's homely story of 45 years' work and play in the Shetlands proves him to have been a man of many parts. His excellent water-colours—the more remarkable since we are told they were painted late in life—show him to have had considerable talent in art as well as medicine. The rugged simple life of the islanders is portrayed as only a man who has lived and worked among them in such intimate association could do it. The very human stories, often full of humour, make good reading. The one of the old lady who noted the date of an observation on her calendar and was thereby able to inform the doctor of the parentage of a child born out of wedlock is a good example. The book has been produced in the Shetlands and bears the stamp of that self-reliance that one attributes to the inhabitants.

Diseases of the Nose and Throat (5th ed. London: Cassell. 1948. Pp. 1004. 70s.).—The late Sir St Clair Thomson was engaged on a comprehensive revision of his book when he died early in 1943, and his work has been continued and completed by Mr. V. E. Negus. The result is a well-produced and informative textbook, elegantly written. The sequence of chapters has been recast, out-of-date text and illustrations have been eliminated, and some sections have been completely rewritten. Full weight is given to chemotherapy. The importance of allergy in nasal disease is emphasised, but the fact that it is common in children (in whom it may be confused with sinusitis) is perhaps not sufficiently accentuated. The use of local anæsthesia alone or combined with thiopentone is not recommended in laryngofissure or laryngectomy, and the extended skin incisions of Gluck and Sorensen are preferred to a single midline incision. A number of other operative steps reveal a conservative outlook, probably desirable in a work of this nature. The book gives a careful account of all the diseases encountered in this region, the commoner conditions getting most space; and the treatment advised follows orthodox lines. Most of the illustrations are good and well chosen.

Digitized by Google

THE LANCET

LONDON: SATURDAY, MARCH 19, 1949

Specialists' Salaries

THE long-awaited "proposed terms and conditions of service of hospital medical and dental staff" have now been released; but, as the title of the memorandum shows, they are still provisional, and they are being published in order that the Joint Committee of Consultants and Specialists may learn the views of those affected. Whatever criticism of details may be offered, the profession's first reaction will be to acknowledge that the new arrangements constitute a generous and beneficent revolution in the financial status of its junior members. Residents will no longer be expected to work for several years for their board alone, or a little pocket-money in addition, and the "trainee specialist," as he is now to be called, will no longer have to depend on private means, coaching, or hack work during his early struggling years. The tough survivors of that process of financial selection may pretend that it was good for them: it is surely better for the nation that the entry to the higher levels of the profession should be widely open to talent, and also that intelligence should be able to afford to marry young. Before we begin to grumble, let us also recognise that the scale of remuneration as a whole is generous. Who would have predicted that a Socialist Government would have been prepared to pay specialists up to £2750 a year for all, and up to £5250 for those of special distinction? In fact the payments to trainee specialists may be initially too generous. For it is proposed to pay these doctors one year after registration over £200 a year more than their junior house-officer colleagues at the same period, and this may have the undesirable effect of encouraging too early specialisation.

The grades of junior and senior hospital medical officer are somewhat negatively defined as well as cumbersomely described. In many types of hospital there are doctors who will come into these categories, but it will not always be true to say that they are not specialists; in which case the establishment will include specialists "who are not of staff specialist status"—for example, many of the medical officers of mental hospitals. Large general hospitals, especially teaching hospitals, need many doctors of this type to do much responsible routine work in the psychiatric, ophthalmic, genito-urinary, venereal, and dermatological outpatient departments, and some of them have specialist status on the staffs of other hospitals. Is it the post or the practitioner that is to be graded? If the former, the anomaly will arise that a doctor is a specialist in one hospital and a hospital medical officer in another. If, on the other hand, the individual is graded, some hospitals will find their specialist staff enlarged by the inclusion of doctors whom they have previously classified as clinical assistants.

Last week's *New Statesman and Nation* contained an open letter to the Minister of Health reproaching him for his preferential treatment of the part-time as compared with the whole-time specialist. The part-timer, it alleges, is prone to neglect his work or to accept pay for sessions he does not attend, or is too anxious to amass sessions now that he is to be paid for them. Yet he is to be paid extra for domiciliary visits and allowed travelling expenses, and income-tax allowances under Schedule D, which are denied to the whole-timer. Perhaps the horns and tails of the part-timers are not so obvious, nor the haloes of the whole-timers quite so bright, as the writer implies. Nevertheless it seems to be true that the proposed terms favour the part-timer. Since he may earn up to $9^1/_2$ elevenths of a whole-time salary, in addition to his fees for domiciliary visits and the various allowances already mentioned, he may well be better off than the whole-timer and still have the right to practise privately. The source of this anomaly is that the Minister's policy in respect of hospital staffing has been one of laissez-faire. Since the balance between whole-time and part-time work in the service has been left to depend on individual choice, the Minister can only wait and see what happens and pay accordingly. The alternative is to decide in advance the ratio most suitable for the service, and regulate the supply of whole-timers and part-timers by varying the financial attractions of the two branches. This may well be impossible at the moment, at least for the country as a whole; but there is much to be said for encouraging regional boards to make local experiments which in time would yield the data on which more far-reaching decisions could be based. Meanwhile there seems no reason to deny the whole-timer his income-tax allowances on books and journals, and it might be wise to reduce slightly the maximum number of sessions which the part-timer is allowed to undertake. It should be noted that whole-timer and part-timer alike are entitled to additional remuneration for such duties as lecturing to nurses, and that both will be paid (by university or medical school) for whatever teaching of medical students and postgraduates they may undertake.

The proposed terms of remuneration must be seen against the background of the cuts in the budgets of the regional boards and the boards of teaching hospitals. Salaries cannot be cut, and there will, therefore, be a tendency to economise by reducing the number of specialists to be paid. Any reduction, on grounds of economy, in the number of trainee specialists would be short-sighted, and the growing demands on the hospital services show that we cannot do with fewer trained men and women. We can only, by better organisation, make the most economical use of those available.

Perhaps the most difficult financial problem that the profession has to face is the allocation of awards for special distinction. Here again we must recognise that the Government has shown both generosity and breadth of vision. The principle of incentives and rewards has been accepted with the general agreement of the profession. To detach the rewards from age and length of service was an act of imagination and perhaps daring. But (many are saying) has not the awards committee been set an impossible task? The answer is that the task will become possible only if

Digitized by Google

we frankly recognise that it is impossible. Distinction is incapable of quantitative measurement: it is a matter of opinion, about which one group of men will differ from another group equally painstaking and fair-minded. It follows that there must always be some recipients who might fairly claim a higher award than they will actually receive. If we recognise this at the outset it may smooth the path of the awards committee; and those who are disappointed can at least console themselves with the thought that after deduction of income-tax and surtax the differences between the awards are by no means as great as they look.

Names for Blood-cells

TODAY most British clinicians and pathologists use the same names for the various cells found in the blood and bone-marrow. Even when the names are not quite the same, the plan of nomenclature is a standard one: for instance some trace the normal development of the red blood-cells from a primitive pro-erythroblast through a series of "normoblasts" of varying maturity; others reserve "normoblast" for the latest stage before the cell loses its nucleus, and use "erythroblast" for the earlier stages. It is agreed that the megaloblasts are a pathological form of developing red blood-cell occurring only in the group of diseases characterised by absence of the anti-anæmic liver principle, or interference with its function. It is agreed that granular leucocytes, lymphocytes, monocytes, plasma cells, and megakaryocytes have separate lines of development from a primitive "blast" stage, through various intermediate developing and distinguishable types to the mature cell. It is also recognised that the bone-marrow contains a very primitive cell—the hæmocytoblast—that probably represents the earliest stage of the red-cell series, the granular leucocytes, the lymphocytes, and the monocytes.

This very considerable measure of agreement has been reached almost imperceptibly in the course of the past ten years. Fifteen years ago the British schools were still talking about the "megaloblast" as the mother cell for all red cells; plasma cells were still thought to be altered lymphocytes; and BARTA's work on the stages of development of the megakaryocytes had gone unrecognised. We do not now intend to describe the history of these changes; they have been brought to the notice of our readers in successive editorial articles in these columns. The stimulus to a more rational nomenclature for blood and bone-marrow cells has come mainly from studies of the sternal marrow, and the fully developed result of such studies can be seen in ISRAËLS's new atlas.[1] Our present nomenclature can be claimed to be more rational because it is based on ideas that have given us a much clearer view of the pathology—both anatomical and functional—and the treatment of many diseases of blood formation.

A system of nomenclature like the one we have outlined is now accepted in all Western Europe, in most of the British Commonwealth, and in South America. To the United States it spread more slowly. Most difficulty arose there over the conception of the megaloblast as a separate pathological series, because the ideas that the megaloblast was the primitive precursor of all red cells, and that in pernicious anæmia red-cell development was "arrested" at the megaloblast stage, had originated in American schools. Later publications from American schools and hospitals, particularly in the Eastern States, showed that the European system was being adopted, and recently a big impetus has been given to the recognition of a "normoblast-megaloblast" type of nomenclature by the demonstration that folic acid, and now vitamin B_{12}, are active only in those patients whose bone-marrow shows megaloblastic erythropoiesis—in the European sense of the term. But, even last year, some American textbooks were published that showed no recognition of these changes in nomenclature, and it was clear that, in the U.S.A. especially, many workers did not accept, or were unfamiliar with, these systems.

It was in these circumstances that the American Society of Clinical Pathologists and the American Medical Association set up a committee under the chairmanship of Dr. E. E. OSGOOD to consider nomenclature and to make recommendations that could be accepted by all and used as a standard—allowing for language variation, perhaps an international standard. The first report, on the leucocytic series, was published last May[2]: it distinguished a "progranulocyte" that nobody had needed before, and no very clear reasons were given for this separation; the spelling of "plasmablast" was oddly preferred to "plasmoblast"; but apart from these minor points, the proposals were generally acceptable. The proposals for the red-cell series were circulated later and have now appeared in print.[3 4] Here the committee thought it necessary to abandon the classical names: their reasons were, first, that the term "megaloblast" had led to so much misunderstanding that they did not want to use it, and secondly that in all other series the suffix "—blast" was reserved for the earliest distinguishable member, and so the red-cell series did not reflect the progress from "—blast" to "—cyte" that was standardised for the leucocytic series. The committee therefore proposed the terms "rubriblast, prorubricyte, and metarubricyte" for what in the nomenclature used by WHITBY and BRITTON[5] and ISRAËLS are "pro-erythroblast, early, intermediate, and late, normoblasts" respectively. The name "erythrocyte" was retained for the mature red clood-cell. For the megaloblast groups the committee proposed to write the term "pernicious-anæmia type" before rubriblast and the rest.

The committee's proposals were discussed at the January meeting of the Association of Clinical Pathologists in London[6], when Dr. ISRAËLS introduced the subject. He accepted the leucocyte proposals in the main, but disagreed completely with the proposed new names for the red-cell series. He argued that confusion about megaloblasts is now limited to certain less senior American schools and hospitals, that the term "rubriblast" is an unpleasant Latin-Greek hybrid, and that use of the prefix "pernicious-anæmia

1. Israëls, M. C. G. Atlas of Bone-marrow Pathology. London, 1948.
2. *Amer. J. clin. Path.* 1948, **18**, 443.
3. *Ibid.* 1949, **19**, January number.
4. *Blood*, 1949, **4**, 89.
5. Whithy, L. E. H., Britton, C. J. C. Disorders of the Blood. London, 1946.
6. *Lancet*, Feb. 26, p. 350.

Digitized by Google

type" is to be deprecated because it tends to prejudge the diagnosis. The subsequent discussion, in which Dr. C. J. C. BRITTON and Dr. A. H. T. ROBB-SMITH took part, showed that the meeting agreed with Dr. ISRAËLS. The proposals have been published in the American journals,[4] but without comment, and it looks as though American opinion about them were divided.

In the face of this opposition, the American committee's proposals are unlikely to gain unanimous acceptance. But the matter will not be left there; a valuable impetus towards greement has been given and discussions will continue. We began by noting how little disagreement really remains on this question of nomenclature. Next year the International Hæmatology Conference will be held in Cambridge; and, surely, with the groundwork so well prepared, there will then be an opportunity for European and American clinicians and pathologists to meet and settle the details of a nomenclature acceptable to all. Not everyone will agree with Dr. ISRAËLS that current usage, however illogical, is a better basis than an unfamiliar set of terms, however uniform. But agreement is probably practicable on such a basis, and we shall be surprised if the agreed standard nomenclature differs much from that in use in so many countries today.

Malignant Hypertension

FEW surgical procedures have achieved so much popularity with so little publicity as lumbodorsal sympathectomy for hypertension. This major development in sympathetic surgery emphasises the need for closer inquiry into both the causes and the effects of high blood-pressure.

With the reluctant sanction of the pathologists, the term "malignant hypertension" has crept rather uncomfortably into our nomenclature, alongside such entities as "thyrotoxicosis" and "idiopathic steatorrhœa." But there are good reasons for uncertainty. Like many other major advances, ALLBUTT's separation of hypertension without renal involvement (hyperpiesia) from renal hypertension led to an over-simplification, so that the exceptions which should have proved the rule and formed the starting-point for the next advance were for many years ignored. When VOLHARD and FAHR took up the thread in 1914 they recognised "malignant nephrosclerosis" as a vascular rather than an inflammatory form of Bright's disease, but their morbid-anatomical bias led them to the view that the endarteritis and arteriolar necrosis found in the kidneys was the cause of the hypertension. By making a more careful study of the disease in its early stages KIMMELSTIEL and WILSON [1] and ELLIS [2] concluded that the clinical syndrome of malignant hypertension with papillœdema preceded the renal lesions, and they put forward the view that renal damage was the result and not the cause of the hypertension. This interpretation did not, however, convince the pathologists, who were unable to accept the "inflammatory" picture of chronic interstitial nephritis as a sequel to hypertension. When WILSON and BYROM [3] provided experimental evidence that induced hypertension in the rat could give rise to renal lesions identical with those of malignant hypertension in man, a clinical-pathological reconciliation appeared inescapable. In this country the evidence has been generally accepted, and much of the obscurity surrounding chronic Bright's disease has been lifted. In America on the other hand, though WILSON and BYROM's experimental results have been confirmed, their views have had only scant acceptance, largely owing to GOLDBLATT's [4] strange insistence that their experimental renal lesions can be explained by pre-existing pyelonephritis. GOLDBLATT was able to produce arterial necroses in his hypertensive dogs only when *both* renal arteries were so severely constricted that uræmia resulted. He maintains therefore that the lesions are due to the combined effects of hypertension and some humoral factor.

BYROM and DODSON [5] have now answered GOLDBLATT's criticism and have provided direct evidence that raised intravascular pressure can by itself produce renal vascular necrosis. By forcible injection of saline into the carotid artery of the rat, these workers intermittently raised the aortic pressure by 80–90 mm. Hg. After several injections they observed irregular residual pallor of the kidney surface, which they attributed to transient vascular spasm. On histological examination of the kidneys, necrotising arteritis was observed in 10 out of 23 rats. Though the lesions were very few (1 or 2 per section), they closely resembled the arterial necroses seen in experimental hypertension: arcuate and interlobular arteries and afferent arterioles were affected but glomerular lesions were not observed. In 10 animals, one renal artery was occluded by a loop of thread during the injection, to protect the kidney against the increased blood-pressure; and no vascular necroses were observed in the kidneys thus protected. Arterial lesions were not found in other organs, but BYROM and DODSON suggest that vascular spasm similar to that observed in the kidneys may occur elsewhere, and that it may account for some of the acute symptoms of malignant hypertension, especially those associated with encephalopathy.

Though these observations do not exclude the possibility that humoral factors or uræmia may in some circumstances contribute to the production of arterial necroses, they afford convincing evidence that these lesions can result from raised intravascular tension alone. In applying the findings to human disease it must be admitted that comparable renal lesions have not followed induction of experimental hypertension in other animals; but the rat approximates very closely to man in the facility with which hypertension can be induced, particularly as a result of unilateral renal damage. Though we still do not know exactly why hypertension leads to renal vascular damage, papillœdema, and encephalopathy in some patients and not in others, the accumulating experimental evidence confirms the clinical concept that fundamentally malignant hypertension differs from benign hypertension only in the height of blood-pressure, and that repeated or persistent elevation of intravascular tension above a "safety" level—which may vary in different individuals—produces irrever-

1. Kimmelstiel, P., Wilson, C. *Amer. J. Path.* 1936, **12**, 45.
2. Ellis, A. W. M. *Lancet*, 1938, **i**, 977.
3. Wilson, C., Byrom, F. B. *Ibid*, 1939, **i**, 136; *Quart. J. Med.* 1941, **34**, 65.
4. Goldblatt, H. The Renal Origin of Hypertension. American Lecture Series. Springfield, Illinois.
5. Byrom, F. B., Dodson, L. F. *J. Path. Bact.* 1948, **60**, 357.

Digitized by Google

sible vascular lesions and thereby leads to a *qualitative* change in the nature of the disease process. Herein the surgeon may find a more satisfactory rationale for sympathectomy and an explanation of some of his results.

Annotations

THE KING

ON March 8 a bulletin was issued by Sir Maurice Cassidy and his colleagues stating that the King's general health continued to be excellent, and that in the left leg the flow of blood had been restored in the main arteries to a satisfactory degree. In the right leg, however, the main artery was still obstructed, and the circulation was being carried on, less efficiently than in the left leg, through collateral vessels. The bulletin concluded:

> "With a view to improving the blood-supply to the right foot, and to safeguard this for the future, we have advised His Majesty that the operation of lumbar sympathectomy should be performed on the right side. The King has accepted this advice and the operation will be performed at an early date."

Last Saturday morning lumbar sympathectomy was carried out at Buckingham Palace by Prof. J. R. Learmonth (assisted by Mr. A. J. Slessor), with Prof. J. Paterson Ross (assisted by Mr. C. J. Longland); the anæsthetist was Dr. John Gillies. Subsequent announcements made it clear that recovery from the operation was proceeding smoothly, and there is every reason to hope that its object will be achieved. Members of the medical profession must all have recognised the grave possibilities of the King's illness as described at its outset, and will therefore have particular reason to be glad that its course has been relatively favourable, allowing the surgeons to choose, and perform at their own time, a therapeutic operation which should improve function.

The names of Mr. Slessor, Mr. Longland, and Dr. Gillies have not appeared in previous bulletins. Mr. Slessor is medical superintendent of, and assistant surgeon to, the Western General Hospital, Edinburgh. Mr. Longland is first assistant in the surgical professorial unit of St. Bartholomew's Hospital, which Professor Paterson Ross directs. Dr. Gillies is director of the department of anæsthetics at the Edinburgh Royal Infirmary.

NEUROLOGICAL DISORDERS IN PERIARTERITIS NODOSA

THE nervous system is fairly often involved in periarteritis nodosa, as recent reports testify.[1] In an investigation of 16 cases of death from this disease, Parker and Kernohan,[2] at the Mayo Clinic, found that in 5 the nervous system was not affected, while in 4 it was affected only in the terminal stages. In the remaining 7, however, neurological symptoms were present from the start of the illness; in 2 the clinical picture was that of an acute infective process in the brain, which was diagnosed as multiple cerebral abscesses; in the 3rd case the condition resembled clinically a rapidly growing glioma; the 4th was of an elderly patient with signs of peripheral and cerebral arteriosclerosis who died of thrombosis of the basilar artery; in the other 3 the peripheral nerves were involved. Studying the records of 29 fatal cases, Lovshin and Kernohan [3] found that in 15 there had been clinical evidence of peripheral neuritis. In 8 this had taken the more characteristic form, termed by these authors "mononeuritis multiplex," in which various individual peripheral nerves are affected either at the same time or at intervals; in the other 7 there was symmetrical polyneuritis without special distinguishing features. In 4 of these 15 patients clear-cut regression of symptoms and signs had taken place, while in the other 11 the peripheral neuritis gradually or suddenly progressed, or remained stationary till death.

Peripheral-nerve involvement is so common in periarteritis nodosa that this diagnosis has to be considered in any obscure case of symmetrical polyneuritis, especially with fever or disorder of other systems such as the renal and alimentary; where individual peripheral nerves are suddenly affected at varying intervals, and especially when there is fever and pain in the muscles, the diagnosis is highly probable. In explanation of peripheral-nerve involvement in this disease two hypotheses have been advanced. The first is that the unknown toxin or pathological agent which affects the arteries acts independently on the nerves; while the second is that anoxæmia arises in the nerve from closure or narrowing of the nutrient arteries. Lovshin and Kernohan have established beyond doubt the existence of this second mechanism. In 15 of 25 cases submitted to necropsy there had been clinical signs of peripheral neuritis; and in each of these the nutrient arteries showed lesions similar to the arterial lesions elsewhere in the body. The changes were most prominent in the small arteries in the interfascicular connective-tissue; and acute, subacute, and chronic arterial lesions were sometimes found at different levels in the same body. The nerve-fibres showed wallerian degeneration, but the most significant finding, which was not uncommon, was the presence of sharply localised infarcts coinciding with the level of maximal vascular damage.

These studies explain clearly the clinical picture of mononeuritis multiplex in periarteritis nodosa; but they do not clarify the origin of the symmetrical polyneuritis which is almost as common in this disease.

1. Leishman, A. W. D. *Lancet*, 1937, i, 803. MacKeith, R. *Brit. med. J.* 1944, i, 139. Miller, H. G., Nelson, M. G. *Lancet*, 1945, ii, 200. Turner, J. W. A., Paterson, J. H. *Ibid*, 1946, ii, 143. Tonkin, R. D., Pulvertaft, R. J. V. *Ibid*, 1948, ii, 291.
2. Parker, H. L., Kernohan, J. W. *Proc. Mayo. Clin.* 1949, **24**, 43.
3. Lovshin, L. L., Kernohan, J. W. *Ibid*, p. 48.

WHERE SHOULD MEDICINE BE TAUGHT?

THERE was a time when medical schools were not affiliated to hospitals; and the change which brought students to the bedside meant a great advance in medical teaching. Dr. C. Fraser Brockington, writing in a Canadian journal,[1] suggests that now another great change is due. In the hospital, life "still revolves around the necropsy and the microscope"; but the emphasis in medicine as a whole is shifting from the pathology of the individual case to "another pathology," as Simon said in his *English Sanitary Institutions*, "than that which our clinics and dead-houses teach us, yet a pathology almost parallel in its teachings"—the social pathology of disease. The hospital sees end-results, and often only selected end-results; for, as Ryle has pointed out,[2] patients in teaching hospitals are admitted because they are "good teaching material"—that is because of the gravity, difficulty, or rarity of their cases. With ætiology and prevention most physicians and surgeons have little serious concern.

The results of failure to prevent disease change with the centuries: thanks largely to environmental advances the student of today sees other diseases than his forerunner of a hundred years ago, when cholera and tuberculosis were rife, and death from septicæmia was a common outcome of surgery. He cannot grasp how many diseases are essentially "social," for, as Ryle notes, many that were once endemic in England—such as cholera, plague, malaria, leprosy, and hookworm—are now aliens, classed as "tropical" or "subtropical" diseases. Their dis-

1. *Canad. J. publ. Hlth*, 1949, **40**, 22.
2. Ryle, J. A. Changing Disciplines. London, 1948.

Digitized by Google

appearance is an interim victory in the long war fought by the public-health services and the forces of social progress—a war with an interminable campaign still ahead of it. It is therefore unfortunate, Dr. Brockington thinks, that the teaching of medicine is still traditionally centred in the hospital; and he believes that someday (though not yet) it must shift to the health centre.

Meanwhile the student must somehow be taught the preventive outlook while "surrounded by sick people and with the elaborate paraphernalia of curative medicine." The General Medical Council in 1936, the Royal College of Physicians in 1943, the Goodenough Committee in 1944, and the British Medical Association in 1944 all advocated this reorientation of the student's teaching; and gradually, as things happen here, the wheel is turning, the revolution is being achieved. The time has come, Dr. Brockington believes, for universities to adopt local health units and use them for the field training of students in medicine, and for research; and he draws attention to a hopeful proposal, in his own area, to affiliate one division in the West Riding health scheme to Leeds University. Like all exponents of a specialty, he is anxious to see thorough training of the young men who enter it, and thinks that this might be achieved by establishing a diploma in social medicine, open only to graduates of registrar standing, and leading to full specialist status. Without necessarily accepting this suggestion, one may agree with his general thesis.

ANTI-HISTAMINE DRUGS IN THE COMMON COLD

AMONG the many and varied theories concerning the pathology of the common cold, allergy has thus far not won much support. This may well be because of the customary separation of vasomotor or allergic rhinitis from acute infectious coryza of virus origin. Yet some of the symptoms of a virus infection of the respiratory tract may be allergic in origin, as Burnet [1] has suggested from his observations on the symptoms following exposure to living attenuated influenza virus. Lately Brewster [2] in America has carried out a clinical trial of the anti-histamine drugs in the common cold, and he uses his results as an argument in favour of the allergic basis of the nasal symptoms.

Brewster's trial of the anti-histamine drugs followed an earlier report [3] of successful results with one of these compounds. Men, women, and children attached to the U.S. Naval Hospital at Great Lakes, Illinois, were urged to report their colds early to one of three clinics established for the purpose. There they were given one of a series of remedies which were used in succession without selection. The anti-histamine drugs chosen were 'Pyribenzamine,' 'Thenylene,' 'Neoantergan,' 'Histadyl,' and 'Benadryl'; and a combination of codeine sulphate and papaverine hydrochloride was given to every sixth patient to provide a control series treated with a standard medicament. At least three doses of 50 mg. of the anti-histamine drug at 4-hour intervals were given by mouth, and a cold was considered to have been aborted or "cured" if all signs and symptoms disappeared within 24 hours of the beginning of treatment and remained absent for at least 48 hours after treatment had ended. Success in aborting the cold with the anti-histamine drugs depended on the stage at which therapy was begun. Thus cures were obtained in 19 of 21 people treated within an hour of the onset of symptoms, 48 of 55 treated within two hours, 116 of 156 treated within six hours, and 165 of 234 treated within twelve hours. The control capsules gave "cures" in 1 out of 2 people treated within an hour of the onset, 5 of 12 within six hours, and 7 of 22 within twelve hours. In none of the controls treated more than twenty-four hours after the onset was benefit obtained, though a few of those receiving anti-histamine drugs at this time were "cured."

The difficulty of establishing a diagnosis within the first few hours of the cold was met by accepting the patient's diagnosis provided that examination revealed no evidence to disprove it. There are many other points about this trial which could be criticised, such as the inequality of the numbers of treated and control subjects and the uniform success of all the anti-histamine drugs, though their therapeutic powers in most other conditions in which they have been used vary widely. Those whose early hours of suffering from the cold are as characteristic as those of the broadcaster whose head began to steam whenever he ate marmalade will no doubt welcome this report. Others who see red whenever the word allergy is mentioned will derive little comfort from it. A word of caution concerning the side-effects of these compounds is needed lest those who try this latest nostrum find the cure worse than the disease. One of the American subjects became disorientated and confused after taking 200 mg. of an anti-histamine drug in four hours. Others complained of drowsiness for which amphetamine was prescribed; we have previously pointed out that this drowsiness might be dangerous in car drivers and others.

1. Burnet, F. M. *Med. J. Aust.* 1943, **1**, 385.
2. Brewster, J. M. *Nav. med. Bull., Wash.* 1949, **49**, 1.
3. Brewster, J. M. *Ibid*, 1947, **47**, 810.

SYSTOLIC MURMURS

"A LOUD systolic murmur at the apex should be considered organic in nature until it can be proved of other origin. The patient should be treated accordingly even when evidence of past rheumatic fever, enlargement of the heart, diastolic murmur, abnormal electrocardiogram, or heart failure is lacking." This advice, which tallies with the experience of life-assurance societies, is given by Master [1] in the light of his war-time service with the U.S. Navy. It is not always easy to decide what constitutes a "loud" systolic murmur, but American workers appear to have found Freeman and Levine's [2] classification satisfactory. This divides systolic murmurs into 6 grades of intensity; and according to Levine [3] himself different observers rarely differ in their terminology by more than one grade. Intensive use of this scale in the late war showed that murmurs falling into grades 3–6 are likely to be associated with organic disease of the heart. Master points out that systolic murmurs of organic origin may be heard only after exercise; so also may a systolic murmur in a healthy person, but here the murmur is never loud and is always transitory. Cardioscopy may also help, although in early mitral disease no abnormality of outline may be detected on screening or in the X-ray film. Two early signs of mitral disease that should always be sought are: (1) diminution of the space beneath the left main bronchus, as seen in the left oblique position, and (2) straightening of the left border of the heart in the anteroposterior position. As to differential diagnosis, most of the other conditions likely to account for a systolic murmur—such as hypertension, thyrotoxicosis, and anæmia—can usually be excluded by careful history-taking and examination. Where there is any question of the supposed murmur being actually a split, doubt may be resolved by a phonocardiogram. A funnel-shaped chest, kyphoscoliosis, or other deformity can also mislead the unwary.

Experts still differ on the mechanism by which murmurs are transmitted. Both Master and Levine emphasise that transmission is mainly a reflection of intensity, and Levine adds that bony structures are the best peripheral conductors. Kerr and Harp,[4] however,

1. Master, A. M. *Arch. intern. Med.* 1948, **81**, 518.
2. Freeman, A. R., Levine, S. A. *Ann. intern. Med.* 1933, **6**, 1371.
3. Levine, S. A. *Brit. Heart J.* 1948, **10**, 213.
4. Kerr, W. J., Harp, V. C. jun. *Amer. Heart J.* 1949, **37**, 100.

Digitized by Google

are of the opinion that "the sounds which are transmitted through bone are of negligible importance as compared with those propagated through the arteries"; and they conclude that the most important tissues in propagation are the myocardium, the blood-vessels, and the blood itself, and that the rate of propagation is that of the pulse-wave. In children, where soft systolic murmurs are commoner than in adults, the problem is more complicated. In 320 children with "functional" systolic murmurs, Messeloff [5] found that the murmur was always in grades 1–3, and was of short duration in 92% of cases; but, he adds, organic murmurs in children may occasionally be faint and short.

Mackenzie and his school in this country may have gone too far in minimising the significance of systolic murmurs; but they were wholly justified in arguing that to subject a healthy child to a life of unnecessary cardiac invalidism is as blameworthy as to overlook organic disease and allow a child with rheumatic heart disease to lead an overactive life; Mackenzie and his successors have liberated a host of healthy youngsters from the tyranny of the stethoscope. Master rightly holds that the same principle applies to young adults. The discovery of a loud systolic murmur betokening organic disease is only the first step; the next is to determine the functional capacity of the heart, and it is on this basis that the patient should be advised; organic heart disease sometimes proves quite compatible with the attainment of a ripe old age—and that without any serious restriction.

HOW TO TELL THE WORLD

"IN selling 'Health,' you start knowing your product is good," Mr. R. W. King remarked at last Monday's symposium on "Informing the Public," arranged—and attended—by the Middlesex Public Health Department. A good slogan, or some other good idea, he said, will always help to sell something worth having; but no idea, however good, will sell a bad product. This reassuring thought was slightly offset by Dr. Charles Hill's earlier reflection that we know very little about the maintenance of good health; and that in any case people much prefer to hear about ill health. He thinks we might make a sound start in health propaganda by teaching human biology in schools to children between the ages of 11 and 16—not with a particular bias towards sex instruction, but as a straightforward school subject. Exhibitions on health subjects, he believes, attract only the converted (apart from the searcher after samples, who will go anywhere). On the whole he was inclined to think that the private talk, preferably given by the doctor, is the most effective form of health teaching, though he had a not unnatural tenderness for the broadcast. Advice on broadcasting from so brilliant an exponent deserves attention: Dr. Hill believes that a speaker on health should talk simply, and be content to use the unambitious jest as it offers, to speak the English he commonly speaks, and to make relatively few points, preferably in a short time. He himself likes to speak for only five minutes. It is certainly essential to be simple, for as Dr. W. Hartston, who arranged the symposium, explained, those to be addressed are mainly simple people. Of a population of half a million recruits whom he examined during the war, and classified in five grades according to intelligence, about a third were in the two lowest grades. Grade 1, he said, needs no health propaganda; grade 2 may; but the bulk of those addressed are in grades 3, 4, and 5. Propaganda must be arranged according to the needs and capacity of these grades. In the past public-health propaganda has not on the whole been good or particularly successful. He reminded the meeting that diphtheria immunisation was first introduced in 1913; and in 1937 we were still getting an annual death-rate of 3000 from diphtheria. Yet expensive, determined campaigns will get results: in 1946 there were only 455 deaths from diphtheria: in Harrow during 1946–48 there were no deaths at all, and in 1948 no *cases* of diphtheria. The plea for simple, human, popular teaching was endorsed by Mr. Macdonald Hastings, editor of the *Strand Magazine*.

The advice of Mr. A. A. MacLoughlin, public relations officer to the Middlesex County Council, on the manners of the official to the citizen, might change the whole mood of the country if it could be widely adopted. As he said, the person who is casually or indifferently received at the county offices will go away with a bias against health teaching which nothing can counteract.

Perhaps the saddest note at the conference came from a dental officer who begged that no propaganda should be initiated on behalf of his profession: it is useless to offer a service when there are not enough dentists to carry it out. He suggested, however, that the public need educating in the prevention of dental caries; and here is the kind of subject that must commend itself to propagandists. "Keep Your Teeth for Life" might be the slogan—if we knew a little more about how to do it.

POSTGRADUATE EDUCATION IN AUSTRALIA

THE great distances which separate the Australian States hinder informal contacts, and an official body with a reliable administrative framework is a valuable link between the scattered medical communities. The committees for postgraduate education in the different States have therefore joined to form the Australian Postgraduate Federation of Medicine. Provision has also been made for similar bodies in New Zealand and elsewhere to become members. The object of the federation is to encourage and advance postgraduate medical education, work, and research, and it looks forward especially to being able to help in arranging visits by lecturers from overseas to all the centres of the continent. Another side of its work will be to offer advice and recommendations to Australian postgraduates when they visit London or other centres abroad. Each year the federation will nominate a State whose postgraduate committee will then elect the federal executive committee. The postgraduate committee in medicine in the University of Sydney are the first to be nominated; Colonel A. M. McIntosh has been elected the first president, and the hon. secretary is Dr. V. M. Coppleson, 131, Macquarie Street, Sydney.

The barony conferred on Sir John Boyd ORR, M.D., F.R.S., in the New Year's Honours has been granted by the name, style, and title of Baron BOYD-ORR, of Brechin Mearn, in the county of Angus.

Dr. James Craigie, F.R.S., has been appointed general superintendent of investigations and director of the central laboratory of the Imperial Cancer Research Fund. He will take up his appointment in August when Prof. W. E. Gye, F.R.S., retires.

Sir Henry Dale, F.R.S., has been elected a life governor of the fund.

The death is announced from Melbourne of Sir Sidney Sewell, a past-president of the Royal Australasian College of Physicians.

THE INDEX and title-page to Vol. II, 1948, which was completed with THE LANCET of Dec. 25, is published with our present issue. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

5. Messeloff, C. R. *Amer. J. med. Sci.* 1949, **217**, 71.

Digitized by Google

Special Articles

HOSPITAL MEDICAL AND DENTAL STAFF TERMS AND CONDITIONS OF SERVICE

HAVING considered the recommendations of the Spens Committee on the Remuneration of Consultants and Specialists, the Ministry of Health has issued the terms and conditions of service it proposes for hospital medical and dental staffs in the National Health Service. These terms and conditions would operate retrospectively from July 5, 1948.

Discussions with the Joint Committee for Consultants and Specialists, which includes representatives of the Royal Colleges, the Scottish Royal Corporations, and the British Medical Association, are still proceeding, and the proposals do not represent final agreement with the profession's representatives. They are being published at this stage for the information of the profession as a whole.

The essential proposals (omitting certain details) are set out below. In considering them it should be noted that:

1. The terms and conditions of service are subject to minor adjustments for Scotland.
2. All salary scales will apply equally to men and women, and uniformly throughout England, Wales, and Scotland.
3. Under the National Health Service Superannuation Scheme, over and above any salary specified here, the employing authority will be paying a contribution, equal to 8% of the salary, into the superannuation fund. The employee's contribution (6%) will be deducted from remuneration.

SPECIALISTS

Main Scale for Staff Specialists at Hospitals, including Dental Specialists

Specialists appointed at age 32: £1700 × 125–£2075 × 150–£2375 × 125–£2750 per annum non-residential.

Specialists appointed at age 31 or earlier to start at £1550 or £1400 respectively.

Specialists first appointed after age 32: the hospital authority to be able to fix the starting salary at any of the four next incremental points in the scale, (i) by reason of age, special experience, and qualifications, or (ii) by reason of age alone, where seniority has been lost because of service with H.M. Forces; provided that the starting salary shall in no case be higher than the specialist would receive on age alone.

Special Distinction Awards

An Advisory Committee on Awards for Consultants and Specialists has been set up to advise the Minister of Health and the Secretary of State for Scotland which specialists engaged in the National Health Service should receive awards for professional distinction, having regard to the desirability that 4% of all specialists in the service should receive the highest award (£2500 per annum in addition to the "basic salary"), a further 10% the second award (£1500 per annum), and a further 20% the third award (£500 per annum). These awards will be paid as an element of remuneration additional to the main scale and will be superannuable.

TRAINEE SPECIALIST GRADES (INCLUDING DENTAL)

Grade 3 (as defined in the Spens report: posts obtained normally not less than one year after registration and held normally for one year only): £670 per annum non-residential.

Grade 2 (posts obtained normally not less than two years after registration and held normally for two years): £775 per annum non-residential in the first year; £890 in the second and any subsequent years.

Grade 1 (posts obtained normally not less than four years after registration and held normally for three years): £1000 per annum non-residential in the first year; £1100 in the second year; £1200 in the third year; £1300 in any subsequent years.

Trainee specialists not to proceed from one grade to another by automatic promotion. Each grade of post demands a distinct level of ability and experience. A trainee specialist in a lower grade to be considered on merit, along with other applicants, for a vacancy in a higher grade.

A trainee specialist holding an appointment in grade 1 and subsequently appointed to a grade 2 post, to be paid the higher salary appropriate to grade 2 (i.e., £890 per annum) while he holds the post in that grade.

OTHER NON-SPECIALIST GRADES

Junior House-officer (including Dental): £350 per annum non-residential for the first post held; £400 for the second post; £450 for the third and any subsequent post. In each case, a deduction of £100 per annum in respect of residential emoluments. Each post to be tenable for six months.

The Minister will be prepared to authorise, in exceptional circumstances, salaries up to £50 per annum higher, where a post cannot be filled otherwise.

Junior Hospital Medical Officers, who have held house-appointments but who are not trainee specialists, and who have less responsibility than other hospital officers of non-specialist status: £700 (for an officer appointed not less than two years after registration) × 50–£1000 per annum non-residential.

Senior Hospital Medical Officers (senior officers performing clinical duties, who are not of staff specialist status but are not trainees): £1300 per annum (at age 32) × 50–£1750 (non-residential), the position on this scale to be determined by age (subject to arrangements in section headed Determination of Salaries &c.).

Medical Superintendents and Deputy Medical Superintendents.—The objective will be to reduce to a minimum the time to be given by medical staff to administrative duties, and to enable them to devote their energies to clinical work in their appropriate grade. Subject to further consideration in the case of mental hospitals and mental-deficiency institutions, medical superintendents and deputies to be remunerated for clinical work as specialists or senior hospital medical officers, according to their grading; for administrative work, to be remunerated at the appropriate rate for hospital administrative staff; where, however, a whole-time officer is engaged almost wholly in clinical work and gives only a small proportion of time to administrative duties, his appropriate clinical remuneration not to be affected.

TRANSFERRED OFFICERS

Officers who were transferred under section 68 of the National Health Service Act, 1946, and who immediately before July 5, 1948, were receiving salaries better than those now introduced, to be entitled to retain their previous salary on a personal basis, for so long as they remain in the same appointment or another appointment of the same or greater responsibility as the one they held at the appointed day; but otherwise to conform to the new rates of remuneration on taking up a new appointment, or on promotion.

PART-TIME APPOINTMENTS, &C.

Part-time Specialist Appointments

Before offering a part-time specialist appointment the board to assess in terms of hours per week what is the average amount of time required by an average practitioner to perform the duties attaching to the post. In assessing the average amount of time to perform the duties attached to the post, to take into account out-patient clinics, ward rounds, operating sessions, laboratory work, and so on, in their hospitals, including occasional visits to outlying hospitals for consultation,

Digitized by Google

diagnosis, or operative work. Also to include time given—e.g., as consultant adviser to the board on special branches of the service or by way of "pastoral visits" to cottage hospitals; and time necessarily spent in travelling from home or private consulting-room (whichever is the nearer) to the hospital or hospitals served (unless the journey is one which he would undertake irrespective of his work for the board). To *exclude* time spent in emergency calls to patients in the beds in their charge (except where any exceptionally heavy liability to recurring emergency work of this sort is anticipated), or in committee work, or in care of private patients in pay-beds or as outpatients. Also to exclude domiciliary visiting, for which special fees are payable.

The object is to express this aggregate number of hours per week as a number of notional "half-days" per week. It will not be necessary at any time to "clock in" the actual number of hours worked on any particular day or in any particular week by any particular specialist—the number of "half-days" is merely the means of expressing the duties attaching to the post in terms which enable remuneration to be calculated without meticulous adjustments up or down from time to time.

To arrive at the number of notional "half-days" from the aggregate of hours so assessed, the total to be divided by $3^1/_2$, the specialist being given the benefit of the marginal overlaps. In other words, the relation of "half-days" to hours to be as follows:

No. of hours weekly	*No. of notional half-days on which salary will be reckoned*
Up to $3^1/_2$	1
Over $3^1/_2$ and up to 7	2
„ 7 „ „ „ $10^1/_2$	3
„ $10^1/_2$ „ „ „ 14	4
„ 14 „ „ „ $17^1/_2$	5
„ $17^1/_2$ „ „ „ 21	6
„ 21 „ „ „ $24^1/_2$	7
„ $24^1/_2$ „ „ „ 28	8
„ 28	9

The part-time salary to be determined by applying to the number of half-days calculated in this way the formula recommended in the Spens report—i.e., the part-time salary to be the following proportion of the whole-time salary appropriate to the specialist:

$$\frac{\text{number of half-days}}{11} + \frac{\text{one quarter of number of half-days}}{11}$$

or

$$\frac{\text{number of half-days}}{11} + \frac{\text{one quarter of (11—number of half-days)}}{11}$$

whichever is the less, subject to the maximum referred to below.

The following is an example of application of above:

A physician divides his time as follows:

Work	*Estimate of time required by an average practitioner*	*Total weekly time (hours)*
2 outpatient clinics	2 hours weekly { +$^1/_2$ hour's travelling in each case*	$4^1/_2$
"Pastoral visits" to cottage hospitals	One day of seven hours fortnightly, including travelling*	$3^1/_2$
Irregular hospital visits	2 hours weekly, including travelling*	2
Charge of beds	9 hours weekly, + $^1/_2$ hour's travelling daily for 6 days*	12
Adviser to board	8 hours monthly	2
	Total	24 = 7 "half-days"

* Travelling time would of course depend on the particular circumstances of the individual concerned.

For this the physician would receive eight-elevenths of the appropriate whole-time remuneration—i.e., $\frac{7}{11} + \frac{(11-7)}{44} = \frac{8}{11}$.

Part-time Appointments as Senior Hospital Medical Officer

The above formula for arriving at part-time salaries to be applied to all part-time appointments as senior hospital medical officer.

Exceptional Consultations

Specialists who have no contract with the board, but who are called in exceptionally to hospitals or clinics for a special visit (e.g., because of their unusual experience or interest) to be paid at the rate of 5 guineas per visit (including any operative work).

As a normal practice, *retired consultants* to be offered honorary (unpaid) appointments in respect of exceptional calls on their services of this kind, which would give them in return the right to use private pay-beds from time to time.

A *general practitioner* not on the staff of a hospital but called in exceptionally to render a specific service in emergency to be paid at the rate of £2 per visit, unless he is debarred from accepting remuneration by his terms of service under part IV of the Act.

Locum-tenens Arrangements

Normally, leave periods to be covered by the normal contract of service providing for practitioners to deputise for each other. Payment at the rate of 5 guineas per half-day, however, to be made to a locum engaged by a board during a specialist's temporary absence when it is impossible to arrange for his work to be adequately performed by other members of the board's staff within the terms of their contract of service.

A locum engaged by a hospital authority during the temporary absence in similar circumstances of a general practitioner holding an appointment on the staff of a hospital to be paid at the rate of $3^1/_2$ guineas per half-day.

Maximum Remuneration for Part-time Appointments

The maximum to be $9^1/_2$ elevenths of the whole-time salary appropriate to the grade. This maximum *not* to include payments made to a specialist in respect of exceptional consultations performed for a board with whom he is not in contract, payments made in respect of work as locum tenens, and payments for domiciliary visits. Where a specialist holds part-time appointments with more than one board, which together are not equivalent to a whole-time appointment, this maximum to apply to the aggregate remuneration from all the boards concerned.

In special circumstances a board, with the Minister's consent in each case, to have discretion to offer a higher rate of part-time remuneration than that normally applicable.

DOMICILIARY VISITS

Payment to be made separately for domiciliary visits by part-time specialists, but no additional payment for whole-time specialists (the basis being that the whole-time duties will be adjusted to include domiciliary visiting where required). Payment to be on the following basis:

Fee for consultation, 4 guineas, with an additional fee of (*a*) 2 guineas where any operative procedure other than obstetric is undertaken or where the specialist uses his own electrocardiograph or portable X-ray apparatus; (*b*) 4 guineas for an obstetric operation. The additional fee of 2 guineas or 4 guineas to be payable once only in respect of each patient for the current illness.

Boards to make payments, additional to the fee for the visit and to the normal travelling and subsistence expenses, of 1 guinea for a journey of 20–40 miles' radius, 2 guineas for a journey of 40–60 miles' radius, and so on, with an additional guinea for every 20 miles.

Maximum remuneration under this head (excluding travelling and subsistence allowances and additional mileage payment) to be 200 guineas in any quarter or 800 guineas in any year, whichever the specialist prefers.

CLINICAL SPECIALISTS ENGAGED IN TEACHING

Whole-time Clinical Posts in Medical or Dental Schools

As already announced by the Chancellor of the Exchequer, the rates of salary to which the University

Digitized by Google

Grants Committee will have regard in making grants to universities are as follows (operating from April, 1, 1949):

Professors.—Within the range of £2250–2750.

Lecturers.—£600 to a maximum within the range of £1500–2000 (or £2500 for posts carrying special responsibility).

Readers.—Within the range of £1500–2000 (or £2500 for posts carrying special responsibility).

In addition holders of these posts to hold an honorary (unpaid) appointment with the appropriate hospital board or boards, but to receive from the board payment of appropriate expenses, like other specialists, for hospital work. Also to be eligible for distinction awards, the additional remuneration being paid by the university or school and reimbursed to them by the board.

Where exceptionally teachers (including part-time clinical professors or heads of university clinical departments) devote a large portion of their time to university work, to be paid the relevant proportion of the whole-time salary and distinction award by the same method as their whole-time colleagues.

Part-time Clinical Teaching Posts

Specialists performing teaching duties concomitantly with, or separately from, their clinical work to be remunerated by hospital boards like other specialists (including distinction awards and expenses) but in addition to be remunerated by the university or school in recognition of their teaching duties at a rate which appears to the university or school to be appropriate to those duties.

GENERAL PRACTITIONERS ON THE STAFFS OF HOSPITALS IN THAT CAPACITY (PART-TIME)

General-practitioner Hospitals (Cottage Hospitals).—Remuneration in respect of services rendered other than those paid for by the executive council: the hospital management committee to create a staff fund by making a payment of £25 per annum for each bed (other than private pay-beds) occupied on the average in the hospital, the fund to be shared among the general-practitioner staff as they may themselves determine. It is expected that general-practitioner hospitals should have an open staff.

Part-time Medical Officers of Convalescent Homes or other Types of Hospital where no other Rate is Appropriate.—£175 per annum per weekly "half-day" up to a maximum of £1575 per annum.

GENERAL DENTAL PRACTITIONERS EMPLOYED AT HOSPITALS

£150 per annum per weekly "half-day" up to a maximum of £1350 per annum.

Where there is no general dental practitioner on the staff of a general-practitioner hospital the general dental practitioners of the district to be allowed at the discretion of the hospital management committee to have their patients admitted to the hospital where inpatient treatment is necessary.

DETERMINATION OF SALARIES PAYABLE FROM JULY 5, 1948

Specialists.—The boards, in carrying out their review of existing staff, to ascertain the age of each specialist and the date on which he first accepted a staff appointment with full clinical responsibility. Assuming there has been no break in service, the salary payable from July 5, 1948, to be the salary which the officer would have been receiving on that date had the above system of remuneration been in operation since the date of his first appointment. In the case of specialists who were first appointed after age 32, the boards, in determining what their starting salaries would have been, to exercise their discretion as they would have exercised it had they been the appointing authority.

Senior Hospital Medical Officers.—Boards or hospital management committees to have discretion to decide at which point in the salary scale for senior hospital medical officers existing staff should start, provided that the starting salary shall in no case be higher than that which the officer would receive were his position on the scale determined by age alone.

Junior Hospital Medical Officers.—Existing staff in this grade who immediately before July 5, 1948, were receiving less than the minimum remuneration for the grade to start at the minimum of the salary scale; and those who were receiving more than the minimum to enter the scale at the salary they were receiving immediately before July 5, 1948, rounded off, at the discretion of the board or management committee, to the next incremental point in the new scale.

INCREMENTAL DATES

In the case of officers holding appointments at July 4, 1948, the incremental date to be July 5; in the case of new appointments or promotions, the date on which the new post was entered into.

PRIVATE PRACTICE AND RETENTION OF FEES

Whole-time officers not to be entitled to enter into arrangements with private patients under section 5 (2) of the Act to undertake private practice. The contract of a whole-time officer normally to provide that he may be called on to treat patients occupying section 5 beds without additional remuneration. A part-time officer to be able to agree with a board that he will treat patients in section 5 accommodation, in return for remuneration by the board, without charging the patients a private fee for his professional services.

Payments for Professional Services not within the Scope of the Hospital and Specialist Service

It has been necessary to consider the question of payments from outside sources to hospitals, and/or to members of hospital and medical staffs, for the rendering of medical reports on patients who are receiving treatment, and for the examination, diagnosis, and rendering of reports on persons referred to hospitals for these purposes only.

All work of this kind to be divided into the following two categories:

I. Work which may properly be regarded as within the scope of the hospital and specialist services provided under section 3 of the Act.

II. Work which cannot be regarded as within the scope of the service but which may for convenience be done at hospitals or by members of hospital medical staff.

The principles on which these two categories may be distinguished are indicated, and illustrated by examples, in a schedule. Category I includes examination and reports on persons referred *from a medical source* for a second expert medical opinion; on persons resorting to or referred to a mass radiography unit; and on offenders referred by court under sections 24 and 26 of the Criminal Justice Act, 1948.

Services in category I to be available free of charge to any person reasonably requiring them. Members of hospital medical staffs to be permitted to provide services in category II, at hospitals or elsewhere, where their provision would not interfere with other hospital activities or with the proper discharge of hospital duties; but services in this category to be available to persons requiring them (including Government departments) only on payment of appropriate charges.

Where hospital laboratory or radiological facilities are used, such charges represent two elements: (*a*) payment for professional services, and (*b*) payment of hospital costs. Where hospital laboratory or radiological facilities are not required, no charge to be made for the use of hospital premises, payment being in respect of professional services only.

Digitized by Google

Whether the practitioner concerned be a whole-time or a part-time officer, all charges in respect of professional services to be retained by him or remitted to him by the board or committee according as the money is received by the practitioner himself or (as is expected to be the more convenient course when the work is done in hospital) by the board or committee.

Where hospital laboratory or radiological facilities are used, one-third of the payment made to be retained by or remitted to the board or committee, in respect of hospital costs.

Other work in category II includes lectures given by members of hospital staffs to nurses, &c., or to the lay public; and services performed by them for Government departments as members of medical boards.

RETIRING AGE

When an officer reaches age 65 his regular contract to come to an end, provided that (*a*) the board may, with his consent, extend his contract of service (or offer a modified contract) for one year or any less period, and so from time to time until age 70, or (*b*) the board may allow him an honorary contract as mentioned above. These ages to be reduced in respect of practitioners who are "mental health officers" under the superannuation regulations.

TENURE OF POST

No fixed period of tenure to be specified in the contract of service of a specialist. Where a specialist felt that his appointment was being unfairly terminated by a board, he would be entitled to send a full statement of the facts to the Minister, who would obtain the written views of the board and place the case before a professional committee (consisting of representatives of the Ministry and representatives of the profession, under the chairmanship of the Chief Medical Officer) for their advice. The committee to have discretion to interview both parties if they thought fit. In the light of their advice the Minister to confirm the termination of services, or direct reinstatement, or arrange some third solution agreeable to the parties concerned, such as re-employment in a different post. This procedure to be completed before the board's decision to terminate the specialist's services was carried into effect.

RESIDENTIAL EMOLUMENTS

The above rates are non-residential. Where an officer is provided with residential or other emoluments by the hospital (i.e., the officer's main hospital), a reasonable inclusive charge to be fixed by the hospital management committee (or board of governors) for the accommodation or other emoluments (including meals), except that the charge for house-officers to be a fixed rate of £100 per annum.

LEAVE

Annual Holiday Leave

Officers in receipt of salaries of less than £1000: at the rate of 4 weeks per annum (in addition to statutory and general national holidays or days in lieu). Officers in receipt of salaries of £1000 or more: at the rate of 6 weeks per annum (in addition to statutory and other general national holidays or days in lieu). In the case of officers performing part-time services, leave entitlement to be based not on the actual salary but on the corresponding whole-time salary rate.

Absence for such purposes as attendance at court, &c., not to be taken into account for the purposes of annual leave.

The annual leave year to run from April 1 to March 31. New entrants to the service to be entitled to annual leave proportionate to the completed months of service during the year of entry, and thereafter on the normal scale.

Compassionate Leave, and any Special Leave other than "Study Leave"

Leave without pay (normally not counting either for increment or pension) to be granted at the discretion of the board. Leave with pay to be granted by the board with the approval of the Minister.

Sick Leave

An officer absent from duty owing to illness, injury or other disability, to be entitled to an allowance as follows:

During first year of service: 1 month's full pay and (after completing 4 months' service) 2 months' half pay.

During second year: 2 months' full pay and 2 months' half pay.

During third year: 3 months' full pay and 3 months' half pay.

During fourth to sixth years: 4 months' full pay and 4 months' half pay.

During seventh to tenth years: 5 months' full pay and 5 months' half pay.

After ten years: 6 months' full pay and 6 months' half pay.

The board to have discretion to extend the application of the foregoing scale in an exceptional case.

Instructions are given for calculating the allowance which, when added to any sickness benefit, injury benefit, compensation payments, or similar payments including allowances for dependants, is not to exceed the officer's normal monthly salary.

Conditions on which sick-leave allowance is to be paid include the following:

An officer who is prevented by his illness from reporting for duty to notify immediately the officer prescribed for this purpose by the employing authority. If his absence continues after the third day, to submit forthwith a medical certificate as to the nature and probable duration of the illness. Thereafter medical certificates to be submitted at intervals of seven days or at such longer intervals as in any case may be decided by the employing authority. On his returning to duty, the officer to submit a medical certificate of fitness if required.

An officer entering a hospital or similar institution to submit a medical certificate on entry and on discharge in substitution for periodical certificates.

A case of a serious character, in which a period of sick leave on full pay in excess of the normal period of benefit would, by relieving anxiety, materially assist a recovery of health, to receive special consideration by the employing authority.

An allowance not to be paid in a case of accident due to active participation in sport as a profession nor in a case in which contributory negligence is proved, unless the employing authority by resolution decide otherwise.

A period of absence due to injury sustained by an officer in the actual discharge of his duty and without his own default not to be recorded for the purposes of this scheme.

The employing authority to be able at any time to require an officer who is unable to perform his duties as a consequence of illness to submit to an examination by a medical practitioner nominated by the authority.

If it is reported to the employing authority that an officer has failed to observe the conditions of this scheme or has been guilty of conduct prejudicial to his recovery and the authority is satisfied that there is substance in the report the payment of the allowance to be suspended until the authority has made a decision thereon, provided that before making a decision the employing authority shall advise the officer of the terms of the report and shall afford him an opportunity of submitting his observations thereon and of appearing, or being represented, before the authority or the appropriate committee. If the employing authority decide that the officer has failed without reasonable excuse to observe the conditions of the scheme or has been guilty of conduct prejudicial to his recovery, then the officer to forfeit his right to any further payment of allowance in respect of that period of absence.

This scheme not to apply to an officer who is required to absent himself from duty following contact with a case of notifiable disease. In such a case the period of absence to be regarded as special leave with full pay.

EXPENSES

Travelling, subsistence, and other expenses to be paid to meet actual disbursements of officers engaged in the

Digitized by Google

service of the board and not to be regarded as a source of emolument or reckoned as such for purposes of pension. In preparing claims, officers to indicate adequately the nature of the expenses involved; claims to be submitted normally at intervals of not more than one month, and as soon as possible after the end of the period to which the claim relates.

Travelling Expenses

Travelling expenses to be paid by the board for any journey in the board's service, provided that

In the case of a *whole-time officer*, expenses incurred in travelling between his place of residence and the hospital where his principal duties lie not to be allowed except as indicated below.

In the case of a *part-time officer*, travelling between his private consulting-room or place of residence and any hospital where he is employed, whichever is the less, to be regarded as a journey in the board's service, provided that no expenses should be allowed for any such journey or part of such journey which would have been undertaken by the officer irrespective of his employment with the board.

Expenses incurred in travelling from holiday leave to duty or vice versa not to be allowed unless the officer was recalled for special reasons.

Taxi or cab fares to be payable only in cases of urgency or in other cases in which transport is reasonably required and an adequate public service is not available, but where these conditions are not fulfilled an officer using a taxi or cab to be entitled to claim the sum he would have been paid had he travelled by public-service vehicle.

An officer making an overnight journey by rail and engaging sleeping-car accommodation to receive the cost, but any subsistence allowance payable to him for that night to be reduced by one-third.

Except where a private car is used, the sum paid not to exceed the amount disbursed—e.g., if the practitioner is entitled to travel first-class but in fact takes a third-class ticket he can only claim third-class fare. First-class fares to whole-time officers with salaries of £760 and over, and part-time officers of corresponding status.

Car Allowances

Officers, whether whole-time or part-time, to be classified as "regular users" or "casual users" according to whether their annual official regular mileage is estimated to exceed 2000 miles or not.

All regular users of motor-cars, of whatever horse-power, to be paid an annual allowance of £52 and 3½*d.* per mile. The annual allowance to be paid by quarterly instalments in advance. The mileage allowance to be paid monthly or quarterly. The annual allowance to continue during absences on annual leave or sick leave or while the car is out of use being repaired or overhauled, except that where any one period of non-user exceeds two months the sum of £4 6*s.* 8*d.* to be deducted for each complete month after the first (e.g., if a car is out of use for 3½ months, £8 13*s.* 4*d.* should be deducted from the allowance).

If at the end of the year it is found that an officer who has been treated as a regular user has not completed 2000 miles, he should not be called upon to repay any part of the annual allowance. This does not preclude review and reclassification of any officer at any time where appropriate.

Casual users to receive no annual allowance, but to be paid 7½*d.* a mile for the first 3120 miles a year and 3½*d.* a mile thereafter.

Where a "regular user" has contracts with more than one board which require him to make a claim to more than one board, the board with whom he has his main contract to be responsible for paying the annual allowance of £52 and for verifying from time to time from the other boards concerned that the officer is still a regular user, all the boards concerned to pay 3½*d.* a mile for actual mileage in the claims appropriate to them.

If an officer uses a private motor vehicle in circumstances where travel by a public service would be appropriate, a mileage allowance of 1½*d.* a mile to be payable irrespective of the type of vehicle.

Where other officers, or members of an employing authority are conveyed in the same vehicle on the business of the National Health Service, and where fares by a public service would otherwise be payable, an allowance of ½*d.* a mile for each passenger to be payable.

The "allowance year" for the purpose of car allowance to be regarded as the year to March 31. In the first year in which an officer is authorised to use his car, a proportionate reduction of the 3120 miles or adjustment of the annual allowance (as the case may be) to be made.

"Public service" refers to railways, steamships, omnibuses, and tramways.

Payment of Mileage Allowances to Whole-time Officers for Journeys from Home to the Hospital where Principal Duties Lie

Where a whole-time officer travels from his home to the main hospital, either before and/or after an official journey, travels direct from his home to the place visited, or returns direct from that place to his home, mileage allowance to be payable for the whole distance travelled, subject to a maximum based on the return journey from the officer's main hospital to the place visited plus 20 miles.

Ordinary mileage allowance to be paid for the distance equal to the return journey between the officer's main hospital and the place visited. The additional 20 miles to be paid for as follows: (i) if the officer is the holder of a current season ticket for travelling between his home and hospital—at the appropriate rate as detailed above; (ii) if the officer is not a season-ticket holder—the appropriate rates less 1½*d.* a mile.

Subsistence Allowances

For officers in receipt of a salary of £760 per annum or over:

An allowance not exceeding 30*s.* to be payable in respect of each night when the officer is necessarily absent from his home or main hospital on the business of the employing authority. The allowance to be reduced to 25*s.* 6*d.* a night after the first 7 nights at one place and to be further reduced after 28 nights if the stay extends beyond that period.

A night allowance to be deemed to cover a single period of absence of 24 hours.

A day allowance in respect of duties not involving a night's absence to be payable at the rate of 3*s.* 6*d.* when an officer is necessarily absent from his home or main hospital for more than 5 hours but not more than 8 hours, and at the rate of 8*s.* 4*d.* when his absence exceeds 8 hours.

For officers in receipt of a salary of less than £760 per annum, the following rates to be substituted:

A night allowance of 24*s.* (18*s.* after the first seven nights and up to a maximum of 28 nights in one place).

A day allowance of 2*s.* 6*d.* for an absence of more than 5 hours and less than 8 hours, and of 6*s.* for an absence exceeding 8 hours.

Payment of the above allowances to be subject to the provisos that day allowance is not to be paid in respect of any period spent at a hospital as part of the normal duties of the officer; that night allowance is not to be paid in respect of any period during which accommodation is provided without charge at a hospital; and that day allowance is not to be paid for any period during which subsistence is provided without charge at a hospital.

Any meals taken by an officer at a hospital in the course of his normal duties to be charged for.

Postage

Boards to reimburse any expenditure necessarily incurred by an officer on postage or telephone calls in the service of the board, through the periodical claim for travelling and subsistence.

Digitized by Google

STUDY LEAVE, CONFERENCES, &c.

"Study leave" to be granted in accordance with the following provisional scheme, which is subject to reconsideration.

General Rules

Study leave must be for the purposes of study (including research), teaching, examining, taking examinations, visiting clinics, or attending meetings or conferences of a wholly scientific or clinical character. Where its purpose is to enable the officer to undertake work for which he will receive fees (e.g., teaching and examining) it should normally be without pay or expenses. Where it is granted with pay the officer must not undertake any remunerative work without the special permission of the leave-granting authority.

Study leave cannot be claimed as a right. It can be added to periods of ordinary leave.

A. *For periods not exceeding 7 days.* (Normally such leave would be granted for periods of 1 or 2 days, but in exceptional cases up to 7 days may be granted.)

1. Without pay or expenses—at the discretion of the hospital management committee or board of governors.

2. With pay but without expenses—at the discretion of the regional hospital board or board of governors, though authority may be delegated to a hospital management committee.

3. With pay and expenses—at the discretion of the regional hospital board or board of governors, subject to the rules governing the payment of expenses.

B. *For periods exceeding 7 days but not exceeding 13 weeks.*

1. Without pay or expenses—at the discretion of the regional hospital board or board of governors.

2. With pay but without expenses—at the discretion of the regional hospital board or board of governors.

Any period of such study leave in excess of 3 weeks will involve a surrender of one day ordinary leave for every additional day of study leave granted—e.g., an absence of 5 weeks will involve the surrender of one week's ordinary leave; a period of 9 weeks' leave will involve the surrender of 3 weeks' ordinary leave. For this purpose ordinary leave, not exceeding 3 weeks in all, may be carried forward from the immediately preceding leave year.

3. With pay and expenses—at the discretion of the regional hospital board or board of governors, subject to the foregoing and the rules governing the payment of expenses.

Not more than one period of leave under B 2 or 3 may be granted to one officer in any one leave year. Where an officer is employed by more than one board the leave must be approved by all the boards concerned.

C. *For periods exceeding 13 weeks.*

1. Without pay or expenses—at the discretion of the regional hospital board or board of governors.

2. With pay but without expenses } to be referred to
3. With pay and expenses } Ministry for decision.

Payment of Expenses

1. Where officers are teaching, examining, attending meetings or conferences or visiting clinics, &c., at the instruction of the regional hospital board or board of governors, no question of study leave arises, and expenses will be paid in the usual way and at the usual rates. Expenses in connexion with taking examinations (fees, travelling, subsistence) will not be paid.

2. Where officers have applied for study leave with pay for any of the normal reasons and the board is of opinion that the leave is of advantage to the service, the cost of travelling and/or subsistence may be defrayed wholly or in part at the usual rates.

3. While it is desired to give regional hospital boards and boards of governors the maximum amount of discretion in the granting of study leave, it is nevertheles necessary to obtain a fairly uniform policy in the matt of defraying expenses. For this purpose boards shou limit their annual expenditure within the budgets alread approved under both heads (i.e., 1 and 2) as follows:

Undergraduate Teaching Hospitals—£800–1200, accordi to size and circumstances.

Postgraduate Teaching Hospitals—up to £1200, accordi to size and circumstances.

Regional Hospital Boards (including hospital managemen committees in the region)—(*a*) Oxford and Cambridg £1200; (*b*) Newcastle, Leeds, Sheffield, Liverpool, Bristo and Wales, £1600; (*c*) Metropolitan regions, Manchest and Birmingham, £2000.

Where the expenditure of a board for 1949–50 is likel to exceed the total stated, and it is not possible to me the additional cost from "free moneys" at the dispos of the board, application should be made for permissio to increase the amount allocated within the budget f these purposes. Regional hospital boards and boards governors may combine to defray the total or part co of an officer's travelling or other expenses.

MEDICAL EXAMINATION ON APPOINTMENT

The passing of a medical examination to be a conditio of appointment of all officers within the scope of t National Health Service Superannuation Scheme, oth than those who are transferred under the Nation Health Service Act. The examining doctor to be aske to certify that the candidate is "free from any physic defect or disease which now impairs his capacity sati factorily to undertake the duties of the post for whic he is a candidate."

STREPTOMYCIN IN BRITAIN

PRESENT ARRANGEMENTS

THE following statement of the conditions for whic the issue of streptomycin is authorised has been issue at the request of the Ministry of Health.

Control of the use of streptomycin is still considere necessary in view of the severe and sometimes permane toxic effects to which it may give rise. It shoul therefore, only be used in conditions where experien has shown that it provides valuable aid, and even th careful dosage is essential. It is also necessary, befo beginning treatment, and during its course, to keep constant watch for the emergence of streptomyci resistant strains, which may occur with great rapidit For details of dosage reference should be made to t report of the Ministry's standing advisory committee tuberculosis.[1]

TUBERCULOSIS

1. *Tuberculous meningitis.*
2. *Acute miliary tuberculosis.*
3. *Tracheobronchial, laryngeal, and pharyngeal tuberculos*
4. *Certain types of pulmonary tuberculosis.*

(*a*) Pulmonary tuberculosis in which the lesion requiri treatment is of recent development, is progressive, and unlikely to benefit from conventional methods (e.g., bed r and/or collapse therapy) alone. The definition would *inclu* rapidly advancing pulmonary tuberculosis, in which immedia collapse therapy would be dangerous or impracticable, a acute "spreads," including those after collapse thera (e.g., postoperative spreads after thoracoplasty). The defi tion would *exclude* old chronic fibroid or fibrocaseous lesio apparently terminal conditions, and primary foci or minim early lesions with favourable prognosis.

(*b*) Pulmonary tuberculosis submitted to lung resection.

5. *Tuberculous wound infections after chest surgery.*
6. *Other sinuses and cutaneous fistulæ of tuberculous orig*
7. *Abdominal tuberculosis*, including tuberculous peritoni and tuberculosis of the alimentary tract, except where su conditions are terminal events.

1. *Lancet*, Feb. 12, p. 273.

Digitized by Google

8. *Genito-urinary tuberculosis.**

(*a*) A minimal renal lesion for which nephrectomy is considered unnecessarily drastic until conservative treatment has been tried.

(*b*) Where, after nephrectomy, the remaining kidney is known to be diseased but is not so grossly damaged that cure is considered impossible.

(*c*) Where, after nephrectomy, there is tuberculous cystitis but the remaining kidney is healthy or little damaged.

(*d*) Tuberculous cystitis of any origin (not only that given in [*c*] above) when accompanied by severe symptoms.

(*e*) Some cases of genital tuberculosis.

NON-TUBERCULOUS INFECTIONS

All non-tuberculous infections due to streptomycin-sensitive, penicillin- and sulphonamide-insensitive, organisms (not only meningitis and septicæmia due to such organisms, as heretofore). It is essential that both diagnosis and treatment should be bacteriologically controlled in every instance. Treatment of non-tuberculous infections is of short duration (usually less than a week) and the amount of streptomycin used for each case is therefore very small. It is usual to supply 10 g. for a case in the first instance. Streptomycin has not proved effective in the treatment of enteric fever and bacterial endocarditis.

The following points should be kept in mind:

Non-tuberculous Genito-urinary Infections

(*a*) The common infections are due to *B. coli*, *Ps. pyocyanea*, and *Proteus*. In past series the infection has been controlled in about half the cases; in the remainder the organism has become resistant, or resistant secondary invaders have appeared.

(*b*) Control of the infection or the development of resistant organisms usually occurs within 48 hours of starting streptomycin.

(*c*) The treatment is contra-indicated in patients with some underlying conditions—e.g., obstruction, calculus, tuberculous infection. In such instances relapses are almost invariable after withdrawing streptomycin.

(*d*) The treatment recommended is 3 g. streptomycin daily in four doses for 48–72 hours. The urine should be cultured daily and organisms tested for streptomycin sensitivity.

Influenzal Meningitis

The most effective treatment for influenzal meningitis is still under investigation by the streptomycin clinical trials (non-tuberculous conditions) committee of the Medical Research Council, and it is urged that doctors having apparently suitable cases should, in the first instance, seek the advice of the nearest Medical Research Council centre.

The following is a list of the present Medical Research Council centres for the investigation of the effects of streptomycin treatment in non-tuberculous conditions:

Sir ALEXANDER FLEMING, Inoculation Department, St. Mary's Hospital, W.2.
Prof. R. V. CHRISTIE, Dunn Laboratory, St. Bartholomew's Hospital, E.C.1.
Prof. CLIFFORD WILSON, Medical Unit, London Hospital, E.1.
Dr. F. R. SELBIE, Bland-Sutton Institute of Pathology, Middlesex Hospital, W.1.
Prof. A. W. DOWNIE, Department of Bacteriology, School of Hygiene, Mount Pleasant, Liverpool, 3.
Prof. R. W. B. ELLIS, University Department of Child Life and Health, 19, Chalmers Street, Edinburgh, 3.
Dr. A. L. P. PEENEY, Queen Elizabeth Hospital, Birmingham.
Prof. C. H. STUART-HARRIS, University Department of Medicine, the Royal Hospital, Sheffield, 1.
Prof. H. B. MAITLAND, Department of Bacteriology and Preventive Medicine, Public Health Laboratory, York Place, Manchester, 13.
Prof. STANLEY GRAHAM, Royal Hospital for Sick Children, Glasgow.
Prof. J. W. MCLEOD, Department of Bacteriology, the School of Medicine, Leeds, 2.
Dr. N. C. GRAHAM, Institute of Pathology, Grosvenor Road, Belfast.
Prof. ALAN MONCRIEFF, the Hospital for Sick Children, Great Ormond Street, W.C.1.
Sir LIONEL WHITBY, Department of Medicine, University of Cambridge.
Sir HUGH CAIRNS, the Radcliffe Infirmary, Oxford.
Dr. R. H. DOBBS, Queen Elizabeth Hospital for Children, Hackney Road, E.2.

* The treatment of this category is at present limited to certain centres, the names of which may be obtained from regional hospital boards.

In England Now

A Running Commentary by Peripatetic Correspondents

FROM the well-nigh perpetual occupation of seeing Mr. Bevan's patients many of us, I fancy, are busy seeking respites. One of mine is road-building. It is not a very posh road—tiddn a turnpike azackly—nor is the job particularly skilled. It consists merely in spreading dumped lorry loads of brick and rubble and covering them with clinker ready for the steam roller; but it is comforting and honest toil. Three of us get down and lend a hand whenever we can, but George is on the job full time.

Proper chap is George. Seventy-two and square built, he just goes on and on and on. You have to tell him when it is time to knock off, otherwise he would work all night and all the next day without noticing. Nobody could call him garrulous. Before giving utterance he ponders carefully, and a remark rolls off the assembly line perhaps twice an hour. When it comes it is generally humorous, often of an Elizabethan bawdiness, and delivered, except for the wicked twinkle in the eye, with a wooden impassivity of face. Served in two wars George has. He enjoyed the South African job which he says were a nice trip, but in the Fourteen Affair he was an infantryman and there was too much of this yur diggin' even for him; and that, you may be sure, means a lot. His habit of working steadily without looking at the clock rather dates him, and so do some of his pronouncements. To help in our task one of us produced a new shovel—a scoop, as we call it. It is a very fine shovel but rather an outsize affair, only to be lifted with difficulty even when unloaded. While the rest of us stood round in respectful silence George took it up and examined it carefully, feeling and handling it like the maestro he is. He grunted non-committally and began to shovel. "Twaddn niver made for no *white* man," he said. But we can't get it away from him. Proper chap is George.

* * *

I have recently taken over a ward in a London hospital and have been struck by the extent to which patients are subjected to investigation and treatment. One woman of 69, suffering from long-standing postprandial epigastric pain and mild hypertension, having exhausted the local facilities for investigation, was transferred to another hospital for gastroscopy. On her return I asked her how she was feeling. Wreathed in smiles, she replied, "Much better, thank you." I then asked the nurse what treatment she had been having. On hearing the following list of drugs I was not surprised that the old lady was feeling better without them.

Tab. phenobarbitone gr. $^1/_2$ b.i.d.
Thyroid extract gr. $^1/_2$ b.i.d.
Dienœstrol 4 mg. b.i.d.
Acid hydrochlor. dil. min. 30 t.i.d.
Penicillin 300,000 units 3-hrly.
Mist. pot. cit. 1 oz. t.i.d.
Mist. pot. brom. 1 oz. nocte.
Charcoal biscuits as required.

Three other drugs had been crossed off the list during her short stay in hospital. I requested that all the others might be crossed off so that we might start afresh. Next day the patient said she was so glad that she did not have to go on taking all these medicines. The improvement has been maintained.

* * *

The use of kitchen scales for weighing always calls for individual technique. Ours have a negative reading of 6–8 ounces which must be allowed for. I was posting my medical books back to my lodgings, laboriously packed in two ex-canned-meat boxes, with winter pants and vests rammed in to steady their contents. At last I struggled along to the post-office with them. The assistant behind the counter hardly looked up from her knitting, even when I hoisted the first parcel on to the scales, so I coughed, loudly and without regard to the advice of the Central Council for Health Education. "Sorry, 's overweight," said the P.M.G.'s respresentative. "Two ounces." "Oh," said I, "is this one all right?" heaving up the second parcel. "Yep, that's just right.

Digitized by Google

But it won't go now. Leave it at your own risk overnight." Thoughts of the crime wave entering the sub-post-office and washing away Rose and Carless, Romanis and Mitchiner, Handfield-Jones and Porritt, Bailey and Love, all at once, at dead of night, so chastened me that I meekly gathered up both parcels, despite protests from biceps and flexors.

At home, suitable adjustments of the kitchen scales showed that the mere dropping of Haultain and Kennedy would satisfy the requirements of the Postmaster General as to weight; so off I went again, this time to a branch office. "Sorry," said the clerk. "We're closed for parcels."

* * *

Cautionary Tale.—George Bulmer Ditherby was a medical student with High Principles. Otherwise he might have reached the shady side of Harley Street. In his clinical examination for the M.B. it never occurred to him to bribe the Case. Yet a Case when bribed may reveal the diagnosis. So G. B. Ditherby, who might have become Sir George Bulmer Ditherby, is now managing a cinema on the Gold Coast.

It happened thus. When Mr. Ditherby, as he was and is, approached the Case there were two half-crowns on the top of the locker beside the bed. The idea of bribery never entered his mind; and he sought to obtain the history of the Case. The Case, a fat, florid man, was not coöperative. In reply to a leading question, he admitted there had been a sharp pain on the right side—"Stitch in the ribs, that's wot it was." Mr. Ditherby knew better. The Case also admitted shortness of breath. Inspection revealed an obese man with spare tyres round his middle. Strong percussion made the right thorax hyper-resonant. Breath sounds were not audible. In fact, nothing was audible. Deep palpation found the apex beat in the left midaxillary line. Mr. Ditherby awaited the examiner.

His examiner was a pleasant middle-aged man who believed in helping the candidate. (The candidate of today is the doctor of tomorrow: a doctor may need a consultant.) "Well, Mr. Ditherby," he said, "and what do you make of this case?" "Spontaneous pneumothorax, Sir. Probably due to a bulla, because he doesn't look like tuberculosis."

Ex.: "Let's talk it over. What symptoms and signs did you find?"

Dith.: "Acute pain in right side followed by dyspnœa and cyanosis. Right thorax hyper-resonant. Absence of respiratory murmur. Being single-handed I was unable to get the bell sound. But if you would be so kind, Sir, as to tap the half-crowns while I listen—I mean auscultate—I . . ."

Ex.: "No, no, we won't bother about that. Incidentally, that sign is not always present. Did you examine the heart?"

Dith.: "Yes, Sir. The apex beat is in the left midaxillary line."

Ex.: "Quite right. What does that suggest?"

Dith.: "Displacement of the mediastinum."

Ex.: "That would be a considerable displacement. What about the heart sounds?"

Dith.: "N.A.D., Sir, I mean nothing abnormal detected." The Case snorted.

Ex.: "Between you and me it's difficult to get physical signs in obese subjects. Well do I know it. I'm sorry but this is a cardiac case—mitral and aortic. Never mind, Ditherby, better luck next time. We all make mistakes."

The examiner was really sorry for Ditherby, and was also a little puzzled. The two previous candidates, stupid looking fellows, had diagnosed the case without difficulty.

Moral.—There are better uses for half-crowns than producing bell sounds.

* * *

The Swedes have a charming habit of unconsciously dropping English faux pas at unexpected moments. It was a lovely afternoon when we arrived in Uppsala, and gazed up at the 14th century Gothic cathedral. Explaining the programme our guide concluded: ". . . and when we have finished I guess we go round si backside and meet my friend, si Archbishop." Ever since, in our thoracic surgery clinic, when we turn the lung over to dissect the inferior pulmonary vein, the remark floats up—"and now to meet si Archbishop."

Letters to the Editor

OBJECTS OF RESEARCH

SIR,—In attacking the suggestion that geriatric should be recognised as a specialty, Dr. Ellman (Feb. 12 invokes those hoary shibboleths—the dangers of ultra specialisation, compartmentalism, artificial divisions, an the rest. It is not clear where he draws the line betwee specialisation and ultraspecialisation, or whether he i opposed to specialisation except when practised b physicians with specialised leanings, though it woul seem that he does object to the development of ne specialties.

I have no personal interest in geriatrics as a specialty and indeed regard age as the least defensible basis for specialty; but I am concerned that in principle ne specialties should be encouraged, for as has often bee said, they are the growing-points of medicine. Unles a culture grows it must wither and die. As I see i specialisation is merely an expedient for increasin knowledge. It is a valuable instrument for this purpose as Fraser remarks in *The Golden Bough*, it is mainl by specialisation that man has raised himself above th level of the savage. Differentiation of function is biological and practical necessity. To attempt to preven it is to court disaster.

The contributions of general physicians to medicin have indeed been great; but nowhere is knowledge s complete that we can afford to ignore, or to suppress the contributions that those who wish to undertak more intensive study may have to offer. What Dr. Ellma refers to as departmentalism and artificial division are temporary but necessary devices for securing bette facilities for more intensive study. Properly used the are the reverse of harmful.

There is little likelihood in my view that anyone wh specialises seriously will fail "to cling fast to the founda tions of medicine." He cannot do otherwise, for in n branch of medicine can one more than scratch th surface without at once being confronted and confounde by the most recondite problems in science. Compart mentalism breaks down a very little way below th surface, but on the surface it has its uses.

I see no danger in specialisation though much in it abuse, and little danger in the multiplication of specia ties, since those that prove redundant will soon disappea There are of course many who, like Dr. Ellman, sincerel believe that the multiplication of specialties is a menac Their sincerity commands our respect though we ma disagree. Unfortunately there are also some—and the are not few—who exploit this doctrine for profession and personal ends. To my mind the constant reiteratio of the alleged dangers of specialisation, by affording pretext for the unscrupulous, is a greater menace.

London, W.1. A. A. OSMAN.

LYMPHOCYTES AND INTRAVASCULAR HÆMOLYSIS

SIR,—I read with interest Dr. Trinick's preliminar communication in your issue of Feb. 5. Leaving asid the question of gamma-globulin production, the morph logical appearance of the cells he describes is possibl open to other interpretation than that of a specif mechanism for detachment of cytoplasmic masses.

In the course of research on the blood-cells of low vertebrates, chiefly fishes, I have observed simil bud-like cytoplasmic outgrowths of lymphocytes, ar also of other blood leucocytes. The blood leucocyt of fishes survive for longer periods than those of mamma when examined in isotonic-saline media, permitting cle observation of their activities. In freshly made suspe sions of blood in saline, examined in hanging drops room temperature, lymphocytes appear as translucen faintly granular bodies with a smooth outline devo of any suggestion of cytoplasmic outgrowths; and t granular leucocytes display active amœboid movement taking up a variety of different shapes, and adherin to the under-surface of the cover-slip. If the preparatio is allowed to stand for half an hour, and then re-examine the leucocytes present a very different appearanc both granular and lymphoid cells now floating free

Digitized by Google

in the saline, the former having adopted a spherical outline and no longer showing any activity. Both granular leucocytes and lymphocytes are seen to have developed small balloon-like protrusions from the cell surface; these protrusions are perfectly translucent and devoid of all granules. It seems reasonable to suppose that we are dealing here with cells which are dead or dying, the cell-membrane losing its differentially permeable character in these localised regions, so that water rapidly enters the cytoplasm and inflates the membrane to form these observed protrusions. Similar protrusions are seen in dying protozoans, as in amœba and paramecium. I have also observed them frequently in lymphocytes in smears of fish blood treated with Leishman's stain-fixative in the usual way, but not in granular leucocytes in the same smear preparations.

There is thus a strong possibility that Dr. Trinick has been dealing with a normally occurring artefact in his preparations. The question might well be resolved by an examination of freshly drawn blood in a hanging-drop preparation on the warm stage, so that the appearance of a living lymphocyte could be observed in conditions as near normal as possible.

Medical School, King's College, Newcastle-on-Tyne. W. T. CATTON
Lecturer in Physiology.

SHEFFIELD REGISTRARS' GROUP

SIR,—I should like to announce through your columns that a United Sheffield Hospitals Registrars' Group was formed here on Feb. 4. The group has received the official recognition and the encouragement of the United Sheffield Hospitals medical committee.

Royal Infirmary, Sheffield. R. S. WEETCH
Secretary, executive committee.

MANAGEMENT OF PEPTIC ULCER

SIR,—In your leading article of Feb. 26, you speak of a growing body of opinion that the regimen usual for ulcer patients is too rigid. You stress the shortcomings of medical treatment, the tediousness and impracticability these days of drastic dieting, the failures of surgical intervention, and the boomerang tendency of prolonged rest and other over-restrictive régimes. Rightly you opine that it is mental rather than physical rest that is important, and you make a passing reference to the frustrations besetting the restless, eager, and ambitious personalities constituting so many of the ulcer-bearing patients.

Many authors have drawn attention to the underlying personalities of these patients; A. T. M. Wilson in this country, and Wolff, Bolen, Draper, and Katz in America, have all stressed factors of anxiety, frustration, hostility, and resentment acting on hypersensitive and hyperactive people, causing the inward direction of strong emotional stimuli. The psychosomatic theory has been reinforced both by psychoanalytic explanation and by the observations of Wolff and Wolff on the mucous membrane of the human stomach in the presence of certain emotional reactions; and others have shown how hypermotility and hyperactivity are evoked by, and recede with, the presence and the absence of anxiety, rage, and other moods.

This is not to claim that the emotional side of all chronic peptic-ulcer patients is always the most important, or the most amenable to treatment. Like so many psychosomatic disorders, sequences rather than causes must be sought. The language of symptoms and the end-results we recognise as disease entities are limited; but there is a multiplicity of factors, constitutional and environmental, that may comprise an ætiology. Suffice to say that there appears to be a close connexion between the psychic side and the gastric function. Wilson goes so far as to remark that "since psychiatric treatment is probably directed to the basic disturbance it may possibly prove more successful in the end."

There is, I think, enough evidence now to justify a careful examination of all such patients (and certainly young ones) for psychogenic factors. A careful psychosomatic history, and an assessment of personality type and of possible operating factors such as anxiety and frustration, should be followed by psychosomatic explanation and efforts to readjust environmental and social influences, over-ambitious aims, and other reaction phenomena. Dieting, frequent small meals, sedation with phenobarbitone, and the use of alkalis with atropine, are all useful at times. But the therapeutic value of rest and sedation should be used only to relax and soothe the body-mind—not to hide and cloak the underlying discontent of the psyche, so leaving the patient still stewing in his own gastric juice.

I recall a woman, aged 48, who had survived three severe hæmatemeses from a chronic gastric ulcer. She was finally persuaded to accept a long and careful medical treatment, after which a consultant of international standing was able to pronounce the ulcer completely healed. That same evening she had another and grave hæmorrhage, a few hours after hearing some very disturbing family news.

The juxtaposition of the emotional life-history of the patient and his symptoms will often make more sense than their attempted association with dietary transgressions or other physical incidents.

I cannot agree that even in the chronic cases there should be "an acceptance of the inevitable," or that the patient should "come to terms with his disability." A young South African who had had asthma all her life came to London for advice, and after examination by chest physician, allergist, and bacteriologist, she was gravely told by them in consultation that she "should learn to live with her disability." It is satisfactory to be able to report that she did not take this consolatory and defeatist advice. She was able to return home after having "learnt to live without her asthma." May not this positive approach have its rôle too in the elucidation of that body-mind disorder we recognise as peptic ulceration? To the two lines of your old song I should add:

I cannot eat but little meat,
My stomach is not good;
The pain I get and oft repeat
Depends upon my mood.
I've always had a strong conceit,
I cannot tolerate defeat,
It all dates back to mother's teat,
And acids all my food.

London, W.1. S. CHARLES LEWSEN.

HEALTH CENTRES NOW?

SIR,—Your article of Feb. 26 in the Act in Action series and "Practitioner's" letter of March 5, both seem to imply that the one thing necessary to ensure smooth operation of the Act is improved waiting-room accommodation.

"Practitioner" mentions the 3-hour wait the patient may have. But what of the doctor? This overworked and underpaid menial will have two surgeries of this length, and some time in between he has to manage all his visits. To do anything to attract more patients will result in the 3-hour surgery lasting for 4 or 5 hours, with a resultant further deterioration in the standard of the work done; for a tired man cannot do good work.

Let us have some sense of proportion—at present sadly lacking in Governmental circles—about this health service. As Dr. Ffrangcon Roberts has said, the potential demand for medical treatment is unlimited. Therefore there must be either an unlimited supply of doctors (which there is not and which in any case the country could not afford) or there must be a deterrent. In the past, financial considerations have been a very satisfactory deterrent. Now the only safeguard is the limited capacity of the waiting-room. If this last remaining bulwark against inundation by those who like something for nothing is removed, the service will break down completely. True, it causes hardship in some cases; but a general breakdown in the service would cause more.

There is one remedy—more satisfactory than any hurried creation of health centres. Let the patient make a token payment at each attendance. Queues will disappear by the elimination of trivialities. The doctor will have time to treat patients with reasonable care and, lastly, he will have the satisfaction of earning in 10–12 hours *nearly* as much as the optician earns in 6.

Silver End, Essex. J. W. NICHOLAS.

Digitized by Google

HODGKIN'S DISEASE

SIR,—Your leading article of March 5 again emphasises the fact—recognised fully by pathologists but not so fully by clinicians—that Hodgkin's disease affects the whole reticulo-endothelial system.

The technique of deep X-ray therapy used by Mr. T. Anthony Green is based on recognition of the pathological picture. Since radiotherapy can only be palliative, intense local treatment to a mass of glands, with severe resultant reactions, is not justified; for lower dosage can achieve the same symptomatic result. The technique adopted in this department (equally effective in other reticuloses, such as the leukæmias) is as follows:

The symptom-producing mass of glands is treated first, using a dosage of approximately 500r tissue in one week, blood-counts being performed before and after treatment. If the patient's condition is satisfactory, the remainder of the body from neck to groins is then treated in strips, the method being referred to as the "step-ladder" technique. Two fields 30 × 12 cm., one anterior and the other posterior, are used to give a dose of 300–500r in one week per strip according to the patient's condition. The blood-count is recorded weekly and whenever possible the strips are treated in consecutive weeks until the whole neck and trunk have been covered. If the patient's condition is poor or the leucocyte-count has dropped significantly, the course can be interrupted at any strip.

By this means an effective dose (which cannot be achieved by the body-bath method) is given to the patient without any severe constitutional effects. It gives long periods of remission without precluding further treatment when required.

R. F. HENDTLASS.

Radiotherapy Department, Royal Northern Hospital and Prince of Wales's General Hospital, London.

PRACTICE OUTSIDE THE SERVICE

SIR,—Would your peripatetic correspondent of two weeks back please give us some grounds for his assumption that the N.H.S. patient who needs 45 minutes of his doctor's individual attention does not, in fact, get it? It seems rather a serious statement to make without the support of direct evidence. I would assure him that the only unhurried thing still left in a doctor's life *is* the examination of the patient and any discussion that may arise from it—in sickness or in health. This is not the occasion for economising in time.

If your correspondent is anxious to reassure himself on this point, I suggest that he ask the patients themselves. I can put him in touch with random selections of our N.H.S. patients representing every income-group from zero to four figures; I feel sure that they would all have something helpful to say about the National Health Service. Armed with such first-hand evidence from people who have personally "suffered" the service, he would be assured of a respectful hearing from us "insiders."

Bagshot. S. GRAHAM.

VEGANIN

SIR,—In his letter of March 5 Professor Alstead agrees that 'Veganin' tablets disintegrate in water and in gastric juice more rapidly than do tab. codein co. (whereas 'Veganin' tablets disintegrate in 20 seconds or less, we have reports of failure of tab. codein. co. to do so in 24 hours); but he claims that this is unimportant, because the tablets should be pulverised. My information is that patients do *not* pulverise analgesic tablets. I can assure him that the solubility of the active ingredients in 'Veganin' is at least equal to that of those in any tab. codein. co.

I would not presume to argue with a professor of pharmacology as to whether a simple addition of the weights of active ingredients decides the effectiveness of an analgesic tablet, irrespective of the balance of the formula, the quality of the ingredients, and the skill and care exercised in production; but the view of practising physicians who have been observing the results for some years may be accepted as evidence. There seem to be very few who use tab. codein. co. in preference to 'Veganin' for themselves and their own families, no many who would do so for their paying patients; an since the Minister of Health stated clearly that prescrip tions under N.H.S. must be for the most effective medi cines, practitioners are increasingly prescribing 'Veganin under N.H.S. too.

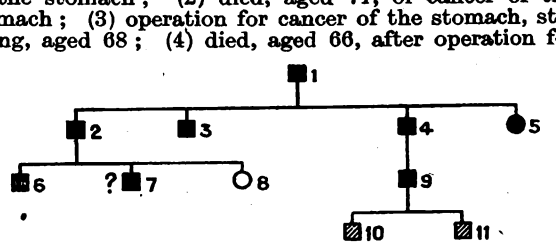
My "indignation," to which Professor Alstead refers was directed to the misuse of our trade-mark 'Veganin which misleads patients into believing that the effects or otherwise, of anonymous tab. codein. co. are attribu table to our product. The professor teaches his pupil that tab. codein. co. are as good; we trust that he wi warn them that these should not masquerade a 'Veganin,' either in hospitals or elsewhere.

The price per 100 quoted by Professor Alstead include purchase-tax, which will not be chargeable on dispensin packs after May 2, and, so far as N.H.S. is concerned, only a transfer from one Government pocket to anothe meanwhile.

William R. Warner & Co. Ltd., London, W.4. ELIOT WARBURTON.

PEPTIC DISORDERS IN A FAMILY

SIR,—The occurrence of gastric and duodenal disorde in succeeding generations of a single family is indicate by the accompanying figure. The following is a summar of the patients' histories: (1) died, aged 72, of canc of the stomach; (2) died, aged 71, of cancer of th stomach; (3) operation for cancer of the stomach, st living, aged 68; (4) died, aged 66, after operation f



Symbols (square = male, circle = female): black = gastric carcinon stippled = duodenal ulcer, unshaded = gastric ulcer.

cancer of the stomach; (5) died in hospital, aged 6 of cancer of the stomach; (6) died of cancer of t stomach; (7) ? cancer of stomach, still living, aged 7 (8) died in hospital of gastric ulcer; (9) operation wh aged 67 for cancer of the stomach, still living, aged 7 (10) duodenal ulcer when aged 39, still living, aged 4 (11) operation for duodenal ulcer when aged 44, st living, aged 48.

The 75-year-old man and his two sons have be patients of mine for the past ten years.

Rayleigh, Essex. C. H. BATEMAN.

THE CUTS

SIR,—The diagnosis of the financial situation present in last week's leading article lacks some of the histo of the case and so may fail to provide a satisfacto basis for treatment. It dates not from the appointed d but from the assurance given by the Coalition Gove ment to the voluntary hospitals that their work sho not suffer through lack of funds. Added to that was extraordinarily generous method of payment for beds be available for emergencies. The first gave the volunt hospitals a sense of financial security such as they h never known before. The second provided them w funds on a large scale so that bank overdrafts disappea to a quite remarkable extent before the end of the w Unlike the municipal hospitals the "voluntaries" kn no kind of budgetary control, with the result that, by the teaching hospitals, they indulged in a financ debauch of which they are now feeling the after-effe Months before the appointed day the more sober-min realised that indulgence on that scale was bound to followed by headaches.

To the suggestion that there must be in the ba ground some system of checking the comparative co the simple answer is "take the figures for 1938 and a reasonable percentage." Even if it is the fancy figur 185% suggested last week in another connexion (p. 4 it will be interesting to see to what extent the accou for 1948 exceed it.

LONDONER

Digitized by Google

DIABETES

SIR,—In your issue of Feb. 5 "Medical Officer of Health" suggests that "every diabetic, however mild, should receive insulin." Few, I think, would agree with him. He then goes on to state that his only complications have been hypoglycæmic attacks, one of which was "provisionally diagnosed" as diabetic coma, for which he was given insulin "pending a blood-sugar estimation."

I do not doubt that the casualty officer or R.M.O. responsible for this unfortunate therapeutic effort thought he was doing the proper thing; but how can even a "provisional diagnosis" of diabetic coma be made in a patient who became suddenly unconscious? Diabetic coma is never of sudden onset; and one has to assume that, as the episode occurred at a medical meeting, a reasonably accurate history was available. It has been the fashion to make light of the dangers of hypoglycæmia, some even holding that death from hypoglycæmia is a clinical curiosity; but recovery from insulin coma may be accompanied by potentially dangerous complications, especially cerebral.

Whereas one can do no harm by the intravenous injection of 30–40 ml. of 50% dextrose into a patient in diabetic coma, one can kill or seriously injure a hypoglycæmic patient by giving him more insulin. And why wait for a blood-sugar estimation? Diabetic coma is due to ketosis and is not the direct result of hyperglycæmia; a catheter specimen of urine is easily and quickly obtained, and if it contains no acetone the coma cannot be diabetic.

I feel that more time could profitably be spent in teaching our senior medical students the differential diagnosis of coma (diabetic or otherwise) and in impressing on them the fact that unconsciousness in a known diabetic patient may be due to causes other than ketosis.

Birkenhead Municipal Hospital. J. L. BLAIR.

POSTURE FOR LIVER BIOPSY

SIR,—The chief danger of needle biopsy of the liver is hæmorrhage, which is sometimes caused by the patient's moving. The patient is usually told to hold his breath while the biopsy is being taken, but sometimes he cannot do so properly throughout the operation. This difficulty can be overcome by adopting the following procedure. The patient sits upright in bed with his knees drawn up and leans forward as far as possible. Radioscopy of 15 patients has shown that in this position there is no respiratory excursion of the lower border of the right lung, and the adjacent posterior part of the diaphragm becomes almost, if not quite, motionless, thus immobilising the liver and making it possible to do the needling easily and without any need for haste. Naturally, care should still be taken to insert the needle only at a site where percussion indicates the absence of intervening intestine. This is usually found between the scapular and posterior axillary lines. If such a site cannot be found, biopsy must be postponed. This method is unsuitable for dyspnœic patients.

Budapest. EMERY SCHILL.

HÆMOGLOBINURIA

SIR,—I believe that Stats, Wasserman, and Rosenthal,[1] whose experience is quoted in your leading article last week, are unnecessarily cautious in recommending that blood-transfusions given to patients suffering from paroxysmal nocturnal hæmoglobinuria should be kept to a minimum. In this disease it seems that the transfused plasma rather than the erythrocytes causes the reactions and exacerbations of hæmolysis that are sometimes observed. If the corpuscles are freed, or almost freed, from plasma by washing the blood with saline before transfusion, reactions appear to be abolished.

I have two patients suffering from this disease who without transfusions become incapacitated by a serious degree of anæmia (erythrocyte-counts about 1,500,000 per c.mm.). For more than a year they have been treated as outpatients, at approximately six-week intervals, with transfusions of the washed erythrocytes derived from 2 pints of blood; and in this way their erythrocyte-counts and hæmoglobins have been maintained at levels allowing them to lead fairly normal lives. In no instance have there been reactions when washed corpuscles have been transfused, and they have travelled home by bus or tube to the other side of London within 30–60 minutes of the transfusions being completed.

Hæmoglobinuria has sometimes, but not always, been abolished by these relatively small transfusions. However, if larger volumes are transfused and the patient's blood-count raised more nearly to the normal level, striking temporary remissions may be obtained.[2]

Finally, two small points in relation to diagnosis. Firstly, the heat-resistance test of Hegglin and Maier,[3] although a useful pointer to a hæmolytic anæmia, is non-specific; quite rapid spontaneous hæmolysis may be observed in other types of severe hæmolytic anæmia. Secondly, Ham's test is better described as an acidified-serum hæmolysis test—not as an acid hæmolysis test. It is not a question of the sensitivity of corpuscles to acid; acid is added to serum before the addition of the suspension of corpuscles only to adjust the pH to the optimum (about 7·0) for the action of the serum factors.

Department of Pathology, Postgraduate Medical School of London. J. V. DACIE.

BACTERIAL WARFARE

SIR,—Your leading article of March 5 provoked thoughts, more widely shared perhaps than expressed, on the identity of aim between old-time magic and modern science. Both propose to learn the "know-how" of the forces of nature, to compel them to serve human ends. As there was a white magic, so there is what may be called a white science, when the powers thus made available are harnessed for human good. But science, like magic before it, is all too prone to be seduced to evil uses.

When in difficulties, the masters of the totalitarian states of the past, the Babylonian and New Egyptian empires, summoned their sorcerers and magicians in the same way as their successors of today call upon the scientists. There is no reason to suppose that modern successors to Daniel and Moses will be lacking to put to rout this improper use of science by an appeal to higher Authority; and considerations such as you have raised do suggest that the medieval idea of the subordination and coördination of all sciences under theology, their queen, may not be as foolish a notion as it may have appeared fifty or a hundred years ago.

Darlington. JOSEPH V. WALKER.

INHALATION OF STOMACH CONTENTS

SIR,—Dr. Willcox's case-histories of inhaled stomach contents during anæsthesia for operative interference of labour, are most interesting and valuable. His warning against a full stomach can be extended to include all cases where the patient feels himself incapable of making a satisfactory reaction to the pressure of painful events.

It is premature to generalise from the beautiful demonstration by A. E. Barclay and F. H. Bentley[4] of arteriovenous shunts under sympathetic control in the gastric submucosa; but it may be that in the stress of anxiety and sympathetic hypertonus an anæmic and functionless mucosa leaves ingested food unchanged and poised for emesis. The traumatised child, bewildered and in pain, is such a subject, as the following cases serve to illustrate.

CASE 1.—A 5-year-old boy received a lacerated scalp while playing three hours after luncheon. Three hours after injury he was anæsthetised with gas and oxygen, and ether. During induction the patient vomited fluid material, some of which he inhaled. Resuscitative measures and bronchoscopy were carried out, but the child died. At post mortem both lungs were congested and the bronchi blocked with food particles.

CASE 2.—A girl of 9 years had lunch at 1 P.M. At 3 P.M. she fell from her pony. She was remounted and rode home

1. Stats, D., Wasserman, L. R., Rosenthal, N. *Amer. J. clin. Path.* 1948, **18**, 757.
2. Dacie, J. V. *Clin. Sci.* 1948, **7**, 65.
3. Hegglin, R., Maier, C. *Amer. J. med. Sci.* 1944, **207**, 624.
4. *Brit. J. Radiol.* 1949, **22**, 61.

Digitized by Google

with a severe supracondylar fracture of the left arm. At 9 P.M. she was anæsthetised with gas and oxygen, and 'Trilene.' During induction she vomited tomato, meat, and solid potato particles. Postural drainage was effective and no vomitus was inhaled.

In attempting to assess the danger of regurgitation during anæsthesia in these cases, the time between the ingestion of food and the onset of the painful occurrence should be taken as the effective digestion time. Thereafter, in the absence of rest and relaxation, the passage of time is no criterion of an emptying stomach; and if an emergency anæsthetic has to be given, the possibility of an artificial evacuation should be considered.

Emsworth, Hants. P. R. BROMAGE.

SIR,—I have read Dr. Willcox's article with considerable interest. I should not agree that inhalation of stomach contents is an unusual accident in these days. It occurs rather too frequently, and the patients are not always fortunate enough to walk out of hospital. I consider that in every case of this kind immediate bronchoscopy and suction should be instituted; it is a life-saving measure. One other point—about Dr. Willcox's 2nd case. Is it not a little unwise to administer thiopentone when one is not certain of an empty stomach? I should like to endorse the opinion that the custom of feeding patients in labour is "risky and should be abandoned."

St. Helier Hospital, Carshalton. HOËL PARRY-PRICE.

A PICTURE SOUGHT

SIR,—A copy of the picture in which Dr. Terence East (Feb. 26) is interested used to hang in the medical outpatient department of King's College Hospital when I was a student there in 1932. The late Dr. A. C. D. Firth used it to impress upon his clerks the importance of the five senses in clinical diagnosis. If, in the course of examining a patient, a clerk had forgotten to look at the tongue and feel the pulse, he was at once sent to look at the picture. It is refreshing to recall those days when diagnoses were made more by clinical acumen than by the filling up of a large number of request forms for intricate investigations.

Aylesbury. RALPH H. GARDINER.

TRICHLORETHYLENE IN LABOUR

SIR,—It is with some hesitation that I enter the controversy over trichlorethylene and its use by midwives,[1] but I have been using 'Trilene' ever since it appeared on the market, for all manner of painful procedures including midwifery. First I employed a modified Clover's apparatus[2]; and since then the 'Cyprane' inhaler, which was kindly lent to me by the makers. The latter is very neat and portable, and has, so far, answered all my requirements in general practice. It does not work on a fixed percentage basis, but it can be locked to give the mixture most suitable for self-induced analgesia for each individual. I do not like fixed-percentage machines and have had no experience of the Freedman.

The Minnitt machines have often proved far from satisfactory. When the first was installed at a county maternity hospital, I offered to give the nursing staff a demonstration of its use.

The first volunteer nurse, seated in a chair, completely lost consciousness after a very short period; but as she was anæmic and rather neurotic I thought that might explain her behaviour, and I proceeded with the second—a buxom type. She too soon began to lose consciousness and I stopped the induction. The third was the sister, a bucolic type with no nonsense about her. She became more deeply anæsthetised than the first, and took much longer to recover consciousness, and her dignity. None removed the finger from the hole, or dropped the facepiece; they first slumped forward, and would have fallen on the floor if I had not prevented it.

After this rather alarming display—for I had previously assured them that anæsthesia was not possible with this machine—I made some inquiries, and w informed that many of those machines had got on to t market wrongly calibrated. Other Minnitt machin erred in the opposite direction in that the percenta of nitrous oxide was too low to give any real relief severe pain. Is it then, I wonder, possible to produ a foolproof machine that is really satisfactory in, if n all, at any rate a large proportion of cases?

Finally, is the average midwife, who has had so training, less competent to supervise self-induc analgesia than the average unqualified dentist, wi no training, is to give full gas-and-oxygen anæsthe to all manner of persons?

Keighley. WRIGHT LAMBERT.

SIR,—I should like to support the excellent letter March 5 from Dr. Hopper. I am strongly in favour of h suggestion that an investigation should be carried o in the homes of the patients, to see whether 'Trilen is really suitable for use by midwives.

New Barnet. JOHN ELAM.

SIR,—The conclusive article of Feb. 26 by I Prescott and his colleagues proves that even the mo recent analgesics reduce the sensitivity of the respirato centre. The article is most timely in view of t proposed issue of analgesia equipment to midwiv and the possible subsequent increase in asphyx neonatorum.

Fortunately, the article shows us a means of counte acting this reduced sensitivity, and of stimulating t respiratory centre. For the experiments the famili 5% carbon-dioxide and oxygen cylinders were used, well as a cylinder with only 3% carbon dioxide. T 5% concentrate was twice as potent as the 3%. Th coincides with the teaching, ten years ago, of Pr Yandell Henderson, who observed that in asphyx neonatorum the respiratory centre was so often desen tised by lack of oxygen that a whiff or two of high concentrated carbon dioxide (even 30%) was needed stimulate it. In other words, carbon dioxide is mo essential than oxygen; and therefore there is no ne for the midwife to carry an oxygen cylinder, for fear asphyxia due to the analgesic.

My large experience of domiciliary midwiv efficiency today gives me confidence to support the iss to them of analgesics, provided that they also carry supply of carbon dioxide.

Hemel Hempstead. GILBERT BURNET.

RETROPUBIC PROSTATECTOMY

SIR,—In prostatic surgery I am an unrepenta "punch" resectionist, but I feel that Mr. Millin is be congratulated on the success of his retropubic ope tion as described in your issue of March 5. I should li however, to comment on one of the conclusions wh have been drawn.

"Earlier operation should be advised in establish prostatic obstruction." This counsel must be int preted with great care. Enlarged prostates vary grea in the degree of obstruction which they produce. In milder degrees the obstruction is overcome by hyp trophy of the bladder, which can be recognised by appearance of trabeculation on cystoscopic examinati It is my practice to treat expectantly all patients w prostatic enlargement and only a small quantity residual urine, unless difficulty in micturition is v extreme. Recently I reviewed those patients of group who had been seen for the first time betw 1938 and 1947.

The series included 129 patients. After a period expectant treatment I have operated on 13 of these patie and 4 others have had operations by other surgeons. remainder show no evidence of increasing obstruction; have been followed for over eight years and 49 for over years. Of the patients examined cystoscopically the majo showed trabeculation of the bladder; in 14 this was nounced, yet only 1 of these has had a progressive co Of these 14, 4 have been followed for about five years; 1 has residual urine amounting to $1^1/_2$ oz., while the remai 3 have smaller quantities.

1. See *Lancet*, Feb. 19, p. 312.
2. Lambert, W. *Brit. med. J.* 1945, ii, 403.

Digitized by Google

It appears that a large proportion of cases of mild prostatic obstruction remain mild and that it is misleading to describe this condition as early prostatic obstruction. If all such cases are treated by operation, many unnecessary operations will be performed. It should be our aim rather to develop those operations which can be applied with reasonable safety to the older patients if the condition has shown signs of being progressive.

Glasgow. T. L. CHAPMAN.

THE NICOTINIC-ACID TOLERANCE TEST

SIR,—The work of Professor Véghelyi and Dr. Sass-Kortsák [1] on the nicotinic-acid tolerance test (N.T.T.) originally described by myself seems to justify the claim that the test has practical usefulness as one of many rapid liver-function tests. However, as I pointed out in my original paper [2] and have confirmed in subsequent studies the results of which will be published in due course, certain qualifications must be attached to the interpretation of the N.T.T.

Firstly, it is as reliable or unreliable as any other liver-function test—that is, it can arouse a suspicion but cannot in itself establish a diagnosis. Like all other liver-function tests, it gauges one of the liver's manifold functions—in this case the inflammatory hepatocellular reaction. In chronic cirrhosis or chronic obstructive jaundice the tolerance will be increased only slightly above the maximum "normal" value, which I arbitrarily set at 200 mg.; responses at 300–400 mg. are by no means unusual in these cases.

Secondly, false positive responses are also not uncommon. There is increased tolerance in tuberculosis (300–500 mg.) without other laboratory evidence of hepatocellular damage; this of course does not exclude the existence of such damage. There is also remarkably high tolerance in herpes zoster and similar neurotropic virus infections, with other liver-function tests only showing slight-to-moderate hepatocellular derangement. Thus all that can be said safely is that increased tolerance justifies a careful clinical check-up of the condition of the liver; and, should other evidence of hepatocellular damage be found, changes in tolerance will gauge the progress of the lesion. It is also safe to assume that a normal N.T.T. result excludes the presence of acute hepatitis.

Regarding the influence of food, I cannot confirm Spear's [3] statement that the time of the last meal would grossly influence the test. On the other hand, I have already pointed out that choline and methionine will decrease the tolerance to normal, or nearly normal, values; I have found since the publication of the original paper that a milk diet (5 pints of skimmed milk daily) will also reduce the tolerance, probably owing to its casein content.

Regarding the mechanism of the test, several explanations are possible, though none is yet proved. The evidence—and especially the influence of choline on the tolerance—seems to indicate strongly that the aminisation of nicotinic acid, contrary to Ellinger's [4] suggestion, does take place in the liver, that in hepatitis the body is raided for liver-protecting amino-acids, and that the increased nicotinic-acid tolerance gauges the excess of amino-acids awaiting disposal by that organ. The fact that the liver prefers the aminisation of nicotinic acid to the other method of disposal—namely, conversion to ammonia and urea—opens up the possibility of therapeutic use of nicotinic acid.

I do not know for certain where in the body nicotinic acid is aminised. Dr. Ellinger suspects that it is in the brain. To quote another authority, Dr. C. H. Best,[5] of the Banting Institute, thinks that it is aminised by and in the liver; otherwise the influence of choline on the N.T.T. could not be explained.

I heartily agree with Dr. Véghelyi and Dr. Sass-Kortsák that the N.T.T. at present is simply a clinical observation that probably opens new avenues for further work.

Toronto. A. ERDEI.

1. Véghelyi, P. V., Sass-Kortsák, A. *Lancet*, Jan. 15, p. 126.
2. Erdei, A. *Ibid*, 1948, i, 368.
3. Spear, G. E. *Ibid*, p. 499.
4. Ellinger, P. *Ibid*, p. 539.
5. Personal communication.

Public Health

Influenza

THERE were 259 deaths from influenza in the great towns of England and Wales during the week ended March 5, compared with 251 in the previous week. Sunderland 7 (12) and South Shields 5 (6) had fewer deaths than in the preceding week, but Bradford 11 (3), Leeds 8 (4), and Manchester 23 (16) had increases; deaths in Greater London were about the same, numbering 89 (85). The figures in parentheses are those for the preceding week. In certain places—e.g., Salford and Leeds—incidence has been very high, but the disease has been of a mild type.

Nearly all the isolations of virus have been of the virus A which was prevalent on the Continent, but virus B has been isolated on eggs from material obtained from two outbreaks in public schools.

Yellow Fever in Panama

The Pan-American Sanitary Bureau has been informed of 8 cases of jungle yellow fever, with 6 deaths, at Pacora, some 25 miles from Panama City. These cases, which occurred last November and December, are the first instances of jungle yellow fever in man to be diagnosed in Panama; no clinical case of urban yellow fever has been seen there for fifty years.

The Future of Mass Radiography

There is still no general agreement on how best to use the many new mass-radiography sets which are promised: and a memorandum[1] prepared by the medical members of the council of the National Association for the Prevention of Tuberculosis, under the chairmanship of Dr. R. R. Trail, will provide a useful basis for discussion. The memorandum first expresses fear that control of mass radiography by the tuberculosis committees of the regional boards may prejudice the preventive value of the service; and with a view to minimising this risk, it is proposed that the statistical findings of all investigations should be communicated to the local medical officer of health. Priority, it is suggested, should be given to groups exposed to the risk of developing chronic respiratory disease, including nurses, doctors, and workers in certain dusty occupations; to entrants to all military and civil services; and possibly to such other groups as secondary-school leavers, food-handlers, and expectant mothers. In each area the local health authority should be consulted on the selection of groups; and patients with any symptoms of respiratory disease should go to clinic or hospital. Under present conditions admission to hospital will often not be secured for cases of early pulmonary tuberculosis detected by mass radiography; and chest physicians to whom such patients are referred "should be pressed to give them clinical and radiological review at least every two months." The unit's director should have charge of beds where he can observe some of the doubtful cases, the remainder being referred to the nearest chest clinic. In mass radiography, it is pointed out, the work is often monotonous; and the director's post should be regarded not as a career but as part of the training necessary for a fully qualified physician to a chest clinic. Similarly, radiographers should be engaged for a period of service with units under the terms of appointment to chest clinics.

The council contends that, with the comparatively few sets now in operation, it is better to concentrate on serial examination of those specially vulnerable than to take groups at random and make no further re-examination for one or two years. With the introduction of B.C.G. vaccination, the calls on the mass-radiography service are likely to increase; and wherever possible, tuberculin skin-testing should be performed when the miniature radiograph is taken. Two possible lines of research are: (*a*) serial radiography and tuberculin testing of closed communities; and (*b*) a follow-up of normal school-leavers over a period of some ten years.

1. *Med. Offr*, March 12, p. 116.

Digitized by Google

Public enthusiasm for mass radiography, the memorandum concludes, seems to be waning; and the association is turning its attention to the production of explanatory leaflets and pamphlets and of posters; it is also considering how best a suitable, realistic film can be made. There is need for lectures and talks, particularly by young people.

Parliament

QUESTION TIME

Fat-content of Ice-cream

Mr. C. W. DUMPLETON asked the Minister of Food what conditions as to the fat-content of ice-cream were made when allocations of sugar were made to the manufacturers.—Dr. EDITH SUMMERSKILL: No such conditions are attached to normal allocations of sugar; but an extra allowance of 15% is granted to manufacturers who undertake to maintain a minimum fat-content of $2^1/_2$%.

Mr. SOMERVILLE HASTINGS: Does the Minister realise what dreadful stuff is now being sold as ice-cream and how small is the fat-content in a great deal of it?—Dr. SUMMERSKILL: I would like to prescribe a standard, but the shortage of milk and milk powder makes it impossible for us to prescribe a satisfactory product, and that is why we have hesitated to do it.

Tuberculosis in the Navy

On March 8 in the House of Commons Mr. JOHN DUGDALE, parliamentary and financial secretary to the Admiralty, in introducing the Navy Estimates for 1949–50 and Navy Supplementary Estimate for 1948–49, said that during the past year 19,700 men had been accepted for the Royal Navy, which was very nearly the Admiralty's target for recruitment. There was one difficulty today which he thought was greater than before the war, and that was the high proportion of wastage. For example, before the war 2 men per 1000 were invalided for tuberculosis. Today they were invalided at the rate of 7 per 1000. This was not due to an increase of tuberculosis in the Navy, but to the fact that there was now a system of examination which enabled the disease to be detected at a much earlier stage.

Patients' Travelling Expenses

Mr. GORONWY ROBERTS asked the Minister of Health why hospital management committees were applying a means test to patients before reimbursing them in respect of travelling expenses between home and hospital.—Mr. A. BEVAN replied: Expenses are payable only in case of hardship, but no means test should be applied. The main test should be the length of journey.

Cremation Certificates

Mrs. C. S. GANLEY asked the Minister whether he would consider fixing a standard fee for doctors and hospitals signing cremation certificates.—Mr. BEVAN replied: I have no authority to fix a standard fee for cremation certificates.

Remuneration for Temporary Residents

Colonel M. STODDART-SCOTT asked the Minister whether it had yet been decided upon what principles doctors in the National Health Service were to be paid for the treatment of temporary residents, visitors, holidaymakers, foreigners, and those patients not on the doctor's list; and how much money was available for this service.—Mr. BEVAN replied: I am still discussing with the profession the principles on which such payments will be made in future. The total amount of these payments depends on the number of persons involved and is a charge on the central pool for the remuneration of general medical practitioners. I have agreed with the profession that payment in respect of the period July 5 to Dec. 31, 1948, shall broadly be on the same basis as under the National Health Insurance arrangements.

In answer to a further question he added that payments for this period would be made on March 31, 1949. These payments were necessarily made in arrear and payment for the period Jan. 1 to March 31, 1949, would be made on June 30, 1949.

Obituary

GEORGE COCKCROFT

M.B. LOND.

THE death of Dr. Cockcroft, of Middleham, on Feb. 2 marks what may be called the end of a dynasty; f he was the last of a line of doctors of his own kin, reachi back to 1780, who practised in this North Riding tow

As a neighbour and friend for over 35 years, I fe qualified to write this notice about him, and, as o privileged to listen to his lecture on 200 Years Country Practice, to write something about this remar able practice, only the first holder of which was different extraction. Those of us who were present this lecture sat enthralled while he described the sequence of these rugged individualists and while he gave extracts from his own poems; and he was a poet of no mean stature. He traced the sequence of only five principals, describing their dress, how they travelled the rough roads, and what remedies they employed (all culled from extant practice records), what they charged for their services, and the detailed accounts they rendered to their patients—the very instruments, still in his possession, which they used. It was an epic deserving wider publication, which his modesty forbade.

George Cockcroft, the son of William Cockcroft, solicitor, was born at Rochdale 1882. He was the grandson of Dr. William Cockcro of Middleham. Educated at Rossall, he went up t school in phenomenally brief time to become head b and gain a scholarship to Guy's Hospital. His hospi career was brilliant, including the award at Guy's the Treasurer's gold medal in clinical surgery, the me and exhibition in anatomy, and the University London medal in medicine and surgery. Everythi pointed to a successful consultant career; but, with philosophy which was already his, he decided to go ba to the family practice in Middleham, the Newmarket the North, at the foot of beautiful Wensleydale. T decision has for more than 40 years meant much Lower Wensleydale. His reward is in the hearts of patients; and those of us, 550 in all, who attended memorial service in St. Mary and St. Alkelda's Chu in Middleham, where Charles Kingsley was the last the canons of the collegiate church, were deeply mo by the obvious place he had in the affections of th whom he had served so long and faithfully.

To spend an hour with him was a memorable exp ence. Subconsciously one would find how deeply ver he was in classical lore, in history (especially that c nected with his beloved dale and his beloved castle), in the science and art of medicine. And then he such a sense of fun. His tales of his years of prac showed this clearly, and with it his kindly attit towards his patients. He was intensely interested and truly loved human beings, and this is what m "Dr. George" the hero of Middleham for more tha generation.

As a neighbouring colleague, I am in a position judge his great professional ability. In country prac we still call upon our neighbours in consultation, never was my confidence in him misplaced. He one of those doctors of whom it can be truly said t he put the welfare of his patients far beyond his professional reputation. He wrote little to the med press, but his friends rejoiced that of late years he so foregone his modesty as to lecture to medical stud and medical societies. His life has been cut short point when his influence would have been great bringing tradition to the rising generation. Also he the only outstanding authority on the history of Wens dale, particularly of Middleham Castle, and his l

Digitized by Google

audiences had the benefit of this, almost to the day of his death.

In the first world war he served in a London field ambulance in Palestine, and was one of the first to enter Jerusalem.

One must not forget his great work as M.O.H., his striving to bring pure water and decent housing to those for whom he was responsible for 42 years, and his especial concern for the care of the aged. His sturdy figure, his abundant white hair, and his singularly charming smile and hearty laugh, will remain long in the memory of those who knew him. It is probable he realised he had not long to live. He once said to me: "A stroke is a grand thing so long as it does its job properly." He worked until an hour before the stroke which rendered him unconscious and brought his life to a close.—This was one of his verses:

"What do you see at end of the road,
That you strain so, Son of mine?
Only the place, where we drop the load,
Fate piled on us, Mother o'mine."

In 1914, he married Mary, daughter of the late Matthew Dobson Peacock, the well-known trainer, and she survives him.

W. N. P.

ETHEL VAUGHAN-SAWYER

M.D. LOND.

Dr. Vaughan-Sawyer, consulting gynæcologist to the Royal Free Hospital, who died at Mount Vernon Hospital on March 9, was born in 1868, the daughter of Cedric Vaughan, J.P., of Millom, Cumberland. After early education at Lausanne and University College, London, she was in 1891 enrolled as the 333rd student of the London School of Medicine for Women. During her undergraduate course she won many prizes and she graduated M.B. with honours in 1896, taking the M.D. two years later. After working at Camberwell Infirmary as assistant medical officer in 1899, she was appointed pathologist to the Royal Free Hospital, and in 1902 assistant physician for diseases of women and assistant obstetrician to the hospital and lecturer in gynæcology in the University of London. On the retirement of Mrs. Scharlieb in 1908 Miss Vaughan became senior gynæcologist and obstetrician. A severe attack of glaucoma compelled her to retire from the hospital and from active surgery in 1928, and despite remissions, her eyesight gradually failed; for the last ten years of her life she was completely blind. She taught herself Braille and continued to live in her house in Harley Street until the last couple of years which were spent in a home where she was happy and received every care.

G. M. S., to whom we owe this memoir, writes: "Many generations of students of the Royal Free Hospital School of Medicine remember Mrs. Vaughan-Sawyer with immense gratitude for her teaching. She was a vivid personality, an excellent diagnostician, and a meticulously careful surgeon. Particularly successful in the performance of Wertheim's hysterectomy for cancer of the ceryix uteri, she used to operate on women whose disease was more advanced than would have been attempted by most surgeons at that time. In those days follow-up clinics for cancer patients were rare, but her cases were seen at regular intervals, and when the disease had recurred she used to send parcels of food and fruit and flowers to her poor women, living mostly in tenements around King's Cross and the Caledonian Road. But her kindness and generosity were unbounded, both to her patients and to her old students and residents.

"Her great success both in hospital and private practice was due to her superb surgical skill, and to the great interest she took in the lives of her patients. This interest remained with her even after her retirement, and she dearly loved a gossip about the doings of her old students and about the affairs of her old medical school and hospital. 'Tottie,' as she was affectionately called, was an essentially human woman. She loved the pleasures of life—good food, good wine, an evening playing bridge—and though often casually, and always unfashionably, dressed she delighted in seeing people smartly and expensively attired. She was a most entertaining conversationalist, with a characteristic chuckle, and her fund of stories, though often unsuited to a drawing-room, never failed to drive home a point to a class of students. It is doubtful whether, at the time, the student always realised how good was her chief's teaching; but once she had started in practice, it was surprising how often she found Mrs. Vaughan-Sawyer had impressed upon her just the facts that were really needed in dealing with women patients. Despite all her family griefs and her progressive ill health, Dr. Vaughan-Sawyer still managed to enjoy the company of her friends, and they were legion. Even within two weeks of her death she was able to say with almost her old sparkle: 'You know, I've had a wonderful life, and am still thrilled when I think about it.' It is this aspect of her personality that will live longest in the memory of those who admired her gallantry so much."

On her marriage to Captain Henry Sawyer, Indian Army, she took the name of Vaughan-Sawyer. Her married life was extremely happy and she never ceased to mourn her husband's death in action in 1914. There was one daughter of the marriage who died in girlhood.

Diary of the Week

MARCH 20 TO 26

Monday, 21st

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. F. S. Gorrill: Anatomy and Physiology of Bone—Part II. (Arnott demonstration.)

HUNTERIAN SOCIETY
7.30 P.M. (Talbot Restaurant, 64, London Wall, E.C.2.) Dr. William Evans, Dr. Geoffrey Bourne, Mr. George Mason: Treatment of Coronary Thrombosis.

Tuesday, 22nd

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. W. E. Gye, F.R.S.: Propagation of Mouse Tumours by Means of Dried Tissue. (Imperial Cancer Research Fund lecture.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Mr. A. K. Monro: Varicose Conditions of the Lower Limb.

CHADWICK LECTURE
4.30 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Dr. Helen Mackay: A Health Service for Children.

ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. Dr. Ronald MacKeith: Visual Aids in Pædiatrics.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Mr. J. C. Trevor: Some Problems of Race.

Wednesday, 23rd

ROYAL COLLEGE OF SURGEONS
5 P.M. Dr. Frank E. Adair (New York): Results of Surgery in the Treatment of Breast Cancer. (Moynihan lecture.)

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Mr. L. Z. Cosin: Social Significance of Geriatric Rehabilitation.

MEDICO-LEGAL SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Miss Rebecca West: Lynching Trials in America.

SOCIETY OF CHEMICAL INDUSTRY
6.15 P.M. *Nutrition Panel* (Gas Industry House, Grosvenor Place, S.W.1). Prof. John Beattie: Effect of Non-protein Calories on the Utilisation of Proteins.

Thursday, 24th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. Kenneth Bowes: Infra-red Photographic Studies of the Superficial Veins in the Female. (Arris and Gale lecture.)

Friday, 25th

ROYAL COLLEGE OF SURGEONS
5 P.M. Dr. W. S. C. Copeman: Pathological Anatomy of Certain Forms of Lumbar Fibrositis and the Rôle of Surgery in its Treatment. (Hunterian lecture.)

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, W.1
8 P.M. Dr. David Nabarro: Congenital Syphilis.

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. H. V. Morlock: Indications for Bronchoscopy in Chest Diseases.

BIOCHEMICAL SOCIETY
11 A.M. (University College, Gower Street, W.C.1.) Short papers.

ROYAL COLLEGE OF PHYSICIANS, 9, Queen Street, Edinburgh
5 P.M. Dr. Ian Hill: Multiple Head Electrocardiograms. (Alexander Gibson lecture.)

Saturday, 26th

ST. STEPHEN'S HOSPITAL, Fulham Road, S.W.10
10 A.M. Prof. Bruce Perry: Ætiology of Acute Rheumatism. (Introductory address to a weekend course.)

Digitized by Google

Notes and News

APPEAL TRIBUNAL

THE membership has now been announced of the tribunal established under the National Health Service Act, 1946, to inquire "into cases where representations are made that the continued inclusion of a person on the list of an executive council would be prejudicial to the efficiency of the service in which that person is participating." The Lord Chancellor has appointed Sir Reginald Sharpe, K.C., to be the chairman of the tribunal. The Minister of Health, after consultation with the associations of executive councils, has appointed Mr. Henry Lesser, O.B.E., LL.B., to be a member of the tribunal. The third member will be selected, according to the profession of the person whose case is being investigated, from the following panel which has been appointed by the Minister after consultations with the organisations representative of the professions concerned: Dr. S. A. Winstanley (medical practitioner), Mr. L. C. Attkins, F.D.S. R.C.S. (dental practitioner), Mr. G. H. M. Graham, M.P.S. (registered pharmacist), Dr. E. G. Mackie (ophthalmic medical practitioner), Mr. W. B. Barker, F.B.O.A. (ophthalmic optician), Mr. J. R. Howard, F.A.D.O. (dispensing optician). The clerk to the tribunal, appointed by the chairman with the Minister's approval, is Mr. R. B. Cooke, solicitor, 5, Verulam Buildings, Gray's Inn, London, W.C.1.

CAMBRIDGE EXAMINATIONS

WITH the help of an advisory committee of Cambridge graduates who hold clinical teaching appointments in the London medical schools and who have been examiners for the final M.B. examination, the faculty board of medicine have considered the recommendations made by the General Medical Council in 1947 on the revision of the curriculum and examinations. The board propose that there should be a rearrangement of the subjects of the two parts of the final M.B. examination. Pathology, pharmacology, and therapeutics are basic subjects necessary for a proper understanding of medicine, surgery, and midwifery and gynæcology, and the board think that as such they should form the subjects of the first part and should be taken after $2^1/_2$ years' clinical study. They consider that the three main clinical subjects (medicine, surgery, and midwifery and gynæcology) should be taken together after 3 years' clinical study and form the second part of the final M.B. examination. They also consider that at the first attempt a candidate should have no option but to take these three main clinical subjects simultaneously, but that a pass should be permitted in one or more subjects provided that a reasonable standard is attained in the remaining subject or subjects. The board also propose that in the first part the scope and character of the examinations in pathology and pharmacology should be the same as for the present examinations in those subjects. Pathology should include bacteriology, preventive medicine from the aspect of communicable diseases, and the pathological aspects of forensic medicine. Pharmacology (including therapeutics and toxicology) should avoid undue emphasis on the academic side of pharmacology and there should be no practical examination. The general form of the separate subjects of the second part should be much the same as the present form of examination in those subjects, but papers in medicine should cover the ancillary subjects—pædiatrics, social medicine, and psychiatry.

INDIAN MEDICAL RESEARCH

THE annual report for 1947 of the Scientific Advisory Board, issued by the governing body of the Indian Research Fund Association, records another year of satisfactory progress. In trials of various preparations of D.D.T. as indoor residual sprays against adult mosquitoes, it was found that a stirrup-pump fitted with a suitable nozzle proved simpler, and answered the purpose better, than other types of equipment. Field trials were conducted, under the ægis of the Calcutta School of Tropical Medicine, to test the action of sulphaguanidine against cholera; this drug acts best during the early stages of the disease. Therapeutic trials with sulphaguanidine, sulphadiazine, and phthalysulphathiazole, conducted under hospital conditions in Calcutta, indicated that sulphaguanidine is the most effective. Three drugs of the sulphone group—'Promin,' 'Diasone,' and 'Sulphetrone'—were tested in the treatment of leprosy at the Tropical School of Medicine, Calcutta, with encouraging results. Although found to have certain limitations, they proved particularly valuable where injections of hydnocarpus oil are not tolerated. Field trials of sulphadiazine and sulphamerazine in bubonic plague were carried out under the direction of the director of the Haffkine Institute, Bombay. Sulphamerazine appears to be the drug of choice, because it gives the desired concentration in the blood with smaller doses administered at less frequent intervals. Streptomycin was tested in experimental plague in animals, with striking results; and its use is being extended to the treatment of plague in man.

The nutritive value of soya-bean milk and soya-bean curd are being examined at the Indian Institute of Science, Bangalore. These are palatable and nutritious, and experimental feeding trials indicate that soya-bean milk and products can provide a reasonably cheap and satisfactory substitute for cow's milk. The government of India have decided to set up a factory in Bombay for manufacturing penicillin and sulpha and antimalarial drugs. Production is scheduled to start in three years' time.

CENTENARY AT WATFORD

ON March 11, 1849, the West Herts Medical Society was formed by a group of seven doctors who met at the Rose and Crown Hotel, Watford. For many years the society was essentially a dining club, but gradually medical topics took pride of place. The town of Watford having grown in size and importance, a separate society was founded there in 1896, but in 1912 this was fused with the senior society.

Dr. C. Herbert Hall, a founder member of the Watford society, and for the past 53 years secretary of this and later of the combined body, was among those who last week attended a dinner held in Watford to celebrate the centenary. Dr. F. M. R. Walshe, F.R.S., spoke of the value of such a body in arousing a sense of continuity with the past, and in promoting mutual regard and respect. Local societies, he observed, become the focus of loyalties which larger associations do not command; and their continuance is vital to the survival of medicine as a humane profession. In his reply, Dr. J. W. Leech, the president, referred to the influence of the Watford society in sustaining a feeling of friendship among the doctors of the neighbourhood. Lord Moran, P.R.C.P., and Sir William Gilliatt, P.R.C.O.G., responded to the toast of The Guests proposed by Dr. F. J. Aldridge.

A G.P. LOOKS BACK

A DOCTOR who can review sixty years of medical life has seen his profession shoot up and branch like the mango tree in the Indian trick. Dr. H. W. Pooler qualified in Birmingham in the days when Jordan Lloyd, his chief, could look up from an amputation to the young man loitering in the theatre in a lounge suit, and say "Now, Mr. Pooler, take your hands out of your pockets and come and hold this leg." In his autobiography,[1] Dr. Pooler sketches pleasantly, if superficially, the great revolution of thought and practice in which he has participated. It is a placid chronicle of steady work and some considerable achievements, starred with agreeable anecdotes and informed throughout by what he describes as his "inveterate optimism"—though it might more fairly be called his confidence that the universe somehow makes sense. When a man who has had more than eighty years of it believes this, the rest of us should not feel disheartened: Dr. Pooler's book is a tonic, elegantly and blandly presented.

University of Oxford

The University Grants Committee have given £193,6[illegible] towards the cost of the erection of a physiology laboratory.

Ophthalmological Society of the United Kingdom

The annual congress of the society is to be held at 1, Wimpole Street, London, W.1, on Thursday, Friday, and Saturday, March 31, April 1, and 2, under the presidency of Mr. F. Juler, who will give an address on the Operation for Acute Glaucoma and on Refraction. The programme also includes a discussion on corneal grafting when the opening speakers will be Prof. A. Franceschetti, Mr. J. W. Tudor Thomas, Prof. G. P. Sourdille, Mr. B. W. Rycroft, and Mr. D. P. Choy[illegible]

1. My Life in General Practice. London: Christopher John[illegible] 1948. Pp. 194. 15s.

Digitized by Google

Royal College of Surgeons of England

At a meeting of the council held on March 10, with Lord Webb-Johnson, the president, in the chair, Hunterian professorships were awarded to Prof. C. F. M. Saint of South Africa and Prof. Robert Harris of Toronto. Prof. W. E. Gye, F.R.S., was elected an emeritus professor of the college from the date of his retirement from the directorship of the Imperial Cancer Research Fund.

A Leverhulme scholarship was awarded to Mr. W. J. Dempster of the Postgraduate Medical School of London. Diplomas in public health were granted jointly with the Royal College of Physicians to P. L. Karney and D. F. van Zwanenberg.

Royal Appointment

Dr. J. L. B. Ansell has been appointed surgeon apothecary to the Royal Household at Sandringham in succession to the late Sir Frederic Willans.

Auxiliary Royal Army Medical Funds

The annual general meeting of members will be held at 11, Chandos Street, London, W.1, on Monday, April 4, at 5.30 P.M.

Royal Microscopical Society

On Wednesday, April 6, at 5 P.M., at B.M.A. House, Tavistock Square, London, W.C.1, Dr. J. A. Murray, F.R.S., will be admitted to the honorary fellowship of the society.

British Schools Exploring Society

Applications are invited for the post of an honorary surgeon for the Northern Norway expedition, leaving on Aug. 3 and returning on Sept. 20. Further particulars will be found in our advertisement columns.

CMF/MEF Physicians

A reunion dinner will be held on Saturday, April 2, at Simpson's in the Strand, with Dr. E. R. Cullinan in the chair. Further particulars may be had from Dr. Arthur Willcox, hon. secretary, 66, Harley Street, W.1.

Alexander Pigott Wernher Memorial Trust

The trustees have lately allocated £60,000 for the use of the Medical Research Council in accordance with the objects of the fund, which are "the prevention and cure of blindness and deafness in the United Kingdom and British Empire, and in particular research in connexion therewith by financing medical men and students within the Empire to study methods and practices in all countries of the world." The fund will ultimately reach about £300,000.

Chair of Pædiatrics for Wales

The council of the Welsh National School of Medicine is submitting to the University Grants Committee a proposal to set up a chair of pædiatrics and child health at Cardiff. The department will be in the charge of a whole-time professor with two senior assistants. Subject to the approval of the governors of the United Cardiff Hospitals 80 beds will be provided at Llandough Hospital and 17 at Cardiff Royal Infirmary. Instruction on the newborn will remain at the obstetric centres at the infirmary and St. David's Hospital.

Residential Club for Hospital Staff

The board of governors of Middlesex Hospital are buying, with part of their endowment capital, the Marlborough Court Hotel, Lancaster Gate, to use as a residential club for some of their staff and students. The charge for the rooms will cover running expenses, and no cost will therefore fall on public funds. Accommodation is planned for 160 people, including medical officers of registrar status, almoners, physiotherapists, radiographers, members of the administrative staff, and women students of the medical and ancillary schools. There will also be room for a few married medical students.

Health Congress at Brighton

At the preventive medicine section of the congress which the Royal Sanitary Institute is holding in Brighton from May 23 to 27, Brigadier H. L. Glyn Hughes will open a discussion on the Hospital and Medical Services. At the conference of medical officers of health Dr. C. Metcalfe Brown will speak on Public Health Research, and Dr. J. Stevenson Logan will introduce a debate For and Against Institutional Midwifery. In the tropical hygiene section Dr. P. C. C. Garnham will read a paper on Modern Concepts in Malaria Control, and Dr. W. Berry on the West African Groundnut Scheme.

Medical Society for the Care of the Elderly

A meeting of this society will be held on April 1 and 2 at Belmont Road Hospital, Liverpool, when Lord Amulree, Dr. J. W. Affleck, and Dr. Marjory Warren will be among the speakers. Further particulars may be had from Dr. Trevor Howell, hon. secretary, St. John's Hospital, St. John's Hill, London, S.W.11.

British Medical Association in Australia

Mr. Victor Hurley, president of the Royal Melbourne Hospital, has been appointed federal president of the B.M.A. in place of Sir Henry Newland, who has resigned after holding office for 20 years.

Mr. Hurley was director-general of medical services in the Royal Australian Air Force during the war. He is a vice-president of the Royal Australasian College of Surgeons.

Scottish Conjoint Board

On March 8 the following, having passed the final examination, were admitted licentiates of the Royal Colleges of Physicians and Surgeons of Edinburgh, and the Royal Faculty of Physicians and Surgeons of Glasgow:

Abd-El-Rahman Azzam, Elspeth V. Beveridge, Mahala M. Beveridge, Andre Carlos, Elizabeth Carwardine, J. C. Cassaglia, S. H. Curry, S. B. Davies, I. M. Downie, K. A. H. Fermie, W. O'C. FitzPatrick, R. M. Gaze, James Govan, J. G. Hart, Mary M. Hay, Lysbeth R. Hurwich, Margaret J. G. Jamieson, J. H. Kennedy, J. J. O'B. Lavery, James Leonard, D. W. Lyon, G. J. McCann, Sushil Mallick, J. C. Marshall, H. P. P. Morris, J. S. Nelson, Joseph Ryan, Samuel Schlifka, J. G. Sheehy, Isidore Tandatnick, Francis Whyte, H. N. R. Wilson, N. W. Wilson, Matthew Wotherspoon, J. C. Wright.

Health Services in Northern Ireland

Speaking in the Northern Ireland House of Commons last week, Captain T. O'Neill, the parliamentary secretary to the ministry of health and local government, said that by January of this year there had been 175,000 applications for dental treatment, and in over 100,000 cases treatment had been completed. While there were grounds for satisfaction here, he added that the considerable outlay in payments to dentists was a matter of concern. Applications continued at a high level. The number of prescriptions dispensed by chemists in January totalled over 370,000 and cost £90,000. If maintained at that level, payments for prescriptions in a full year would exceed £1 million. By Dec. 1, 120,000 persons had had their sight tested. The cost of the supplementary eye services was expected to be £285,000 greater than was estimated.

Medical Society of London

Presiding over the 169th anniversary dinner on March 8, Dr. T. Jenner Hoskin recalled some of the vicissitudes through which the society had passed since its foundation in 1773. In 1805 what was now the Royal Society of Medicine was founded by dissident members, largely because their president had held his position for 22 years. At first the members were 30 physicians, 30 surgeons, and 30 apothecaries, and the president was always a physician; but for more than a century the physicians and surgeons had alternated in the chair. In its fourth home, in Chandos Street, occupied since 1871, the society was now flourishing, with assets around £30,000. Meetings were very well attended, and, as Lettsom the founder desired, they gave practitioners frequent opportunities of congregating to discuss interesting cases or to communicate discoveries made at home or abroad. Mr. Bernard Darwin, the principal guest, felt that it was a work of supererogation for a layman to propose the health of a medical society, and spoke of the serenity he had gained through having to give up golf. The golfing temperament was not what it was in the days when a player said to his erring putter "you little brute, don't presume on my good nature any longer" and beat it to pieces on a wall; or when another laid all his clubs carefully on the rails in front of an approaching train. The golfer had a niggardly habit of trying to cure his diseases without professional advice; "and on the whole I believe he's right." However, professionals were now giving lessons to groups of youngsters simply for the good of the game, which seemed to be the beginning of a free Golfing Medical Service. Mr. E. W. Riches, proposing The Visitors, recalled that Mr. Darwin's forebear, Erasmus Darwin, was a physician at Lichfield; but legend said that he was paid a guinea a line for his verse, which he probably preferred to a guinea a mile for his visits. Lord Moran, in praising Mr. Darwin as golfer and writer, remarked that happiness consists in finding out what you want to do and doing it all the time—preferably in the open air. He related some of his own experiences "before I made the discovery that I was a natural non-golfer."

Digitized by Google

World Health Organisation

The executive board has accepted the following draft programme and budget of W.H.O. for 1950:

(1) The regular budget, totalling $8,150,110, comprising administrative expenses and an operating programme to be financed by contributions from all members according to the constitution.

(2) A supplemental operating programme of advisory and technical services in the amount of $13,619,180. Governments would be invited to come to the second World Health Assembly prepared to make additional contributions to W.H.O. in order to finance this programme on a basis to be determined by negotiations.

The programme will be submitted to the second World Health Assembly which meets in Rome on June 13.

The Working Party, who drew up the programme, had decided by 4 votes to 3 against budgeting for supplies to governments. In supporting this principle Dr. K. Evang (Norway) pointed out that supplies in the amount of $2 million would be allotted to the demonstration teams initiating public-health programmes. It was also unanimously agreed that W.H.O. would supply governments in emergencies. Moreover, W.H.O. had already created a medical supply bureau to advise governments on how to procure medical and public-health equipment. The question was whether W.H.O. should become truly a supply agency. The Working Party, Dr. Evang concluded, had decided that this was not an essential function of the organisation, and believed that the obtaining of these commodities was basically an economic problem. Dr. Melville Mackenzie (U.K.) while recognising the critical need for health and medical supplies in many areas of the world, felt that W.H.O. should use its influence to assist governments in utilising existing international economic machinery to obtain supplies. He warned that a chaotic situation might ensue if W.H.O. undertook procurement and distribution of health supplies in addition to its other functions. On the other hand Dr. A. Stampar (Yugoslavia) declared that a state of emergency existed now and would continue for several years in many countries, especially in Europe. Unless W.H.O. recognised this fact and acted accordingly, it might mean the end of the organisation.

After further discussion it was decided, by a vote of 14 to 1, that W.H.O. would provide medical supplies to governments. The text of the decision was as follows:

The board is of opinion that it is not within the province of W.H.O. nor is it possible for the organisation to make itself responsible for supplies to different countries. But the board recognises that it may be desirable in some cases for supplies to be made available for specific projects examined in advance in detail and approved by the executive board, either to continue the implementation of programmes after the W.H.O. demonstration teams have finished their task, or to implement or further a health project to be carried out by a governmental health administration. Governments will pay for these supplies wherever possible

The budget for 1950 makes provision for the following projects: mental health ($942,550), environmental sanitation ($1,090,290), tuberculosis ($632,720), venereal diseases ($791,135), mother and child health ($1,114,040), cholera ($177,215), nutrition ($408,285), public-health administration ($488,690), typhus ($181,315), and plague ($209,965).

The mental-health programme, which is the first international plan of its kind, has been prepared according to recommendations made by the World Federation of Mental Health. It includes the collection and dissemination of information, field surveys in rural communities, in industrial units, and among students, and 6 travelling seminar teams to demonstrate methods of survey, prevention, and treatment of mental disorder.

The appropriation for the tuberculosis research programme to evaluate the effectiveness of B.C.G. vaccination has been increased from $100,000 to $300,000. The board has also recommended the convening of an international conference on immunisation procedures as soon as possible, to bring together epidemiologists, pædiatricians, and vaccine experts to discuss the use of new techniques for producing more effective vaccines and to elaborate plans for the widespread application of immunisation.

The board decided unanimously that a regional organisation for Europe should be established in the near future, as soon as the majority of governments concerned agree upon it. It will be recalled that a special office for war-devastated countries in Europe was set up in Geneva on Jan. 1, 1949.

Ecuador has joined W.H.O., bringing the number of member nations to 59.

Prof. G. Grey Turner has been elected an hon. foreign member of the Société de Chirurgie de Lyon.

Appointments

ANDERSON, D. E. W., M.R.C.S., D.P.M.: deputy medi superintendent, Royal Earlswood Institution, Redhill, Surr
ARONSON, R. P., M.B. Lond., M.R.C.P.: pædiatric registr Nottingham Children's Hospital and Nottingham City Gene Hospital.
BRAMLEY, G. F., M.D. Leeds, D.P.H.: county M.O. and school M Gloucestershire.
BRYAN, H. S., M.R.C.S.: medical director, central child psychiat clinic, Alder Hey Hospital, Liverpool.
CAMPBELL, I. D., M.B. Edin.: M.O., Leeds Regional Hospital Boa
CRANNA, D. D., M.B. Manc., F.R.C.S.: asst. orthopædic surge Salford Hospital Centre.
MIDDLEMISS, J. H., M.D. Durh., D.M.R.D., F.F.R.: director of rad diagnostic department, United Bristol Hospitals.
PIRRIE, G. D., B.A., M.B. Camb., D.P.H.: a senior M.O., public-hea department, London County Council.

University College Hospital, London:

AMULREE, Lord, M.A., M.D. Camb., F.R.C.P.: asst. gene physician i.c. chronic sick wards at St. Pancras Hospital.
MERRINGTON, W. R., M.S., B.SC. Lond., F.R.C.S.; asst. gene surgeon.
WOLFE, H. R. I., M.S. Lond., F.R.C.S.: asst. general surgeon.

Hospital for Sick Children, Great Ormond Street, London:

ARNOTT, D. C., M.B. Lond., D.C.H.: registrar, department physical medicine.
ARTHURTON, M. W., M.B. Lond., D.C.H.: house-physician.
BLAXLAND, P. J., M.B. Lond., F.R.C.S.: surgical registrar.
CHAMPION, E. P., M.B.: junior anæsthetics registrar.
CRAWSHAW, E. G. A., M.B. Camb., M.R.C.P., D.C.H.: asst. med registrar.
DAWSON, R. L. G., F.R.C.S.: part-time surgical registrar.
FATHI, J. T., M.S. Lond., F.R.C.S.: part-time surgical registrar
HOPE, E. V., B.A., M.B. Camb., F.R.C.S.: part-time surg registrar.
JOLLY, H. R., M.A., M.B. Camb., M.R.C.P.: asst. medical registra
LOVEL, K. W., M.A., B.M. Oxfd: asst. medical registrar.
MACKENZIE, ALICE, M.D. Aberd.: asst. medical registrar.
MACLEAN, W. E., M.D. St. And., M.R.C.P., D.C.H.: asst. med registrar.
MACOUN, S. J. R., B.A., M.B. Camb., M.R.C.P.: asst. med registrar.
MANN, T. P., M.D. Lond., M.R.C.P., D.C.H.: asst. medical regist
NIXON, H. H., M.A., M.B. Camb., F.R.C.S.: surgical registrar.
PERCIVAL, R. H., M.A., B.M. Oxfd, F.R.C.S.: surgical registrar.
PUGH, J. P., M.B. Birm., M.R.C.P., D.C.H.: asst. medical regist
SAVAGE, T. R., M.A., B.M. Oxfd, M.R.C.P.: asst. medical regist
STANFIELD, MARGARET, M.B. Lond., D.C.H.: asst. med registrar.
VULLIAMY, D. G., B.A., M.B. Camb., D.C.H.: asst. med registrar.
WILLIAMS, D. I., M.A., M.CHIR. Camb., F.R.C.S.: part-t surgical registrar.

Births, Marriages, and Deaths

BIRTHS

ARONSON.—On March 7, in London, the wife of Dr. R. P. Arons a daughter.
BARCLAY.—On March 7, at Middlesbrough, the wife of Dr. P. Barclay—a son.
BURGE.—On March 3, in London, the wife of Mr. Harold Bu M.B.E., F.R.C.S.—a son.
CHETWYND.—On Feb. 28, the wife of Dr. J. B. Chetwynd—a so
CONDON.—On March 8, the wife of Dr. H. A. Condon—a daug
JORDAN.—On March 4, at Sheffield, the wife of Dr. Arthur Jord a daughter.
MANNING.—On Feb. 20, in Belfast, the wife of Dr. F. E. B. Man —a son.
MARSHALL.—On March 6, at Banstead, Surrey, the wife of Dr. J Marshall—a son.
PORTCH.—On March 1, at Caythorpe, the wife of Dr. G. G. Port a son.
STANNING.—On Feb. 16, at Milford-on-Sea, Hants, to Dr. Kath Stanning (née Gillett), wife of Mr. John Stanning—a son.
TAYLOR.—On Feb. 17, in London, to Dr. Jill Taylor (née Weathe wife of Mr. R. W. Taylor—a son.
THOMAS.—On March 7, the wife of Dr. Merley Thomas—a son.
THURLOW.—On March 3, at Axminster, the wife of Dr. G. Thurlow—a daughter.
WHARTON.—On March 5, at Colwyn Bay, the wife of Dr. D Wharton—a daughter.
WILLCOX.—On March 5, at Leamington Spa, the wife of Dr. J Willcox, M.C.—a daughter.

DEATHS

BUCK.—On March 9, Arthur Herbert Buck, F.R.C.S., aged 79.
FRENCH.—On March 5, at Burgh Heath, Ronald Edgar Fre M.A., M.D. Camb.
HAY.—On March 9, Alexander Robertson Forrest Hay, M.B. Gl aged 66.
HAYWARD.—On March 12, at Wilton, Wilts, John Arthur Hayw M.D. Lond., F.R.C.S., M.R.C.P., aged 83.
MARTIN.—On March 12, Alfred Eugene Martin, M.A., M.D. Ca aged 74.
MEADE.—On March 5, at Harrogate, Warren Meade, M.R aged 74.
VAUGHAN-SAWYER.—On March 9, at Northwood, Ethel Vaughan-Sawyer, M.D. Lond.
WEST.—On March 6, at Fleet, Hants, John Weir West, C.B., C. C.B.E., major-general, A.M.S. retd.
WYNNE.—On March 7, at Northiam, Sussex, Walter W M.B. Edin., aged 81.

Digitized by Google

STATE LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

AT THE CROSS-ROADS

THE DEVELOPMENT OF OUR HEALTH SERVICES*

A. LESLIE BANKS
M.A. Camb., M.D. Lond., F.R.C.P., D.P.H.
A PRINCIPAL MEDICAL OFFICER OF THE MINISTRY OF HEALTH

THERE are two periods in English history which at first sight appear to be completely divorced from each other but which to students of social welfare present not only interesting contrasts but a thread of unity.

In A.D. 597 Augustine introduced Christianity to England, and from that time until the dissolution of the monasteries by Henry VIII in 1535–37, the principles of medieval Christianity held sway. From the health point of view the faults were many. The contempt for personal cleanliness, the dis-regard, indeed dis-esteem in which family life was held, combined with a degree of credulity amounting to unquestioning belief in the supernatural, tended to produce a state of mind in which scientific inquiry could not exist. Application of the principles of hygiene, and indeed any rational procedures in medicine, were therefore impossible. On the other hand, the Christian virtue of charity as a thing good in itself, and not necessarily to be practised as an insurance policy against purgatory after death, had important repercussions on the care of the poor and sick. At its height there developed a true brotherhood and spirit of sacrifice one for another which has never been seen to the same extent since that time. It showed itself particularly in the organisation of infirmaries and hospitals associated with the great monasteries, and in the development of the male and female nursing orders, both military and secular, which did such impressive work for the sick during the Middle Ages.

The Reformation destroyed the last remnants of these brotherhoods in England, and the commercial age began. From that time, measures to protect the public health were passed mainly as a means of self-preservation. Hospitals were developed *pour encourager les autres*. Thus, St. Bartholomews' Hospital was, in the 16th century, a place wherein the sick poor might remain, and if need be die, "which else might have died and stoncke on the eyes and noses of the Citie."

It is true that the first Public Health Act had been passed in 1388 and that the beginnings of a Ministry of Food had appeared early in the 16th century with the setting up of a central corn administration on London Bridge; but the lack of public opinion, combined with the ignorance of all classes, prevented any real progress. Meanwhile, there had been a steady development of commerce and the "covetous and insatiable cormorants" of Sir Thomas More became more and more a dominating factor in English life. About the year 1760 the invention of power-driven machinery came to their aid and thus began what has been described as the Industrial Revolution. It was of course merely an industrial acceleration. Many descriptions abound of conditions among the working classes of that time. Thus in one mill known as "Hell Bay" the workers for two months worked every day from 5 A.M. to 9 P.M., in addition to working all night twice a week. The growth of factories led to an ever-increasing demand for labour, and about 1760 the London poor-law authorities sent 20,000 children, of the average age of seven, to work in the mills and factories of Lancashire, Derbyshire, and Nottinghamshire. These children worked the same hours as the adults for six days a week, and on Sundays from 6 A.M. until noon they cleaned the machinery. A special strapper was usually employed to keep them at work. Similar conditions of child labour prevailed in the mines.

These appalling conditions led to the beginnings of modern social reform 150 years ago. The first Factory Act was passed in 1802 and the second in 1819; this limited the hours of work for those under sixteen years of age to a twelve-hour day with one hour overtime; but it was not until 1833 that the salaried factory inspector and the certifying surgeon appeared.

From the beginning of the last century the efforts of the reformers were supported by the trade unions and the coöperative societies and by an ever-growing body of public opinion. This public opinion arose from mixed motives of genuine pity and self-interest. It was this aspect of self-interest which Chadwick played upon so forcibly and effectively.

THREE STAGES

Our modern health services have developed since that time in three stages.

The first was concerned with environmental hygiene—such matters as the disposal of excreta, the purity of water-supplies and food-supplies, the abatement of overcrowding, better provision of air and light, and the control of infectious disease. The peak was reached with the great Public Health Act of 1875 and the results of this and allied Acts began to appear in full measure toward the end of the 19th century.

The next stage was the development of personal health services and arose from a different cause. After the Boer War an Inter-Departmental Committee on Physical Deterioration was set up, and its report, together with the reverses of the Boer War and the low standard of physique of the recruits thereby revealed, led to speedy action. Statutes to provide for a school medical service, to improve the maternity and child welfare services, and to introduce a limited form of national insurance were all in existence before the outbreak of the first world war in 1914. The subsequent extension of these services and the care devoted to the prevention and treatment of the venereal diseases and tuberculosis are too well known to require description.

The third stage is now in progress. This century has seen three great wars and remarkable and costly advances in medicine, surgery, and allied sciences. Finally the recent war has expedited a social and financial revolution. As a result the last few years have seen comprehensive social legislation placed upon the statute-book. To give only some examples, the Education Acts of 1944 and 1946, the National Insurance Act, the National Assistance Act abolishing the Poor Law, the Disabled Persons Act, and the Children Act form part of this comprehensive legislation. For medical services these Acts depend on the National Health Service Act of 1946. This is described in the preamble as an Act to provide for a comprehensive health service for England and Wales, and it is indeed comprehensive in its scope.

THE FUTURE

It may, therefore, fairly be claimed that the social machinery is almost complete. The citizen has now security, a healthy environment, and a long expectation of life. Infant mortality—that sensitive index of the national health—shows an 81% improvement since 1910 for the last three months of the first year of life. It may be asked, therefore, what remains to be done.

There are two main tasks. The first is to improve the existing services to their maximum degree of efficiency. This is in essence a matter of coördination. To give only one example, hospital, local-authority, and general-practitioner services require to be closely coördinated if an efficient and economical service is to be provided for the patient. The second task is to educate the people to use these services wisely and unselfishly.

There are, of course, a number of immediate problems to be dealt with. Thus the arrangements for the care

* Inaugural lecture delivered on Feb. 12 in a course arranged by the Central Council for Health Education.

Digitized by Google

tigrolysis. For this reason many of the reports of chromatolysis are valueless. Again, the interpretation of morphological findings in the Nissl substance is difficult for two further reasons:

(1) The type and appearance of the granules vary in the different nerve-cells. In general, somatic motor cells have large granules throughout the cytoplasm; autonomic cells show large granules round the edges only; and sensory nerve cells display widespread dust-like fine granules.

(2) The fixative used is important. Hopkins (1924) has shown that the size and degree of definition of the Nissl granules varies greatly according to the fixative used. Mixtures of 95% alcohol and 10% formalin in equal parts or 10% formalin containing 2–5% acetic acid, or Zenker's fluid containing 2–10% acetic acid, give the best results. Formalin alone was used by us.

In our cases importance was attached to Nissl-body findings only in body A, because necropsy of body B was delayed for 18 hours. The stain used was dilute alkaline Giemsa with differentiation in absolute alcohol and colophonium. Various degrees of tigrolysis were found in the cerebellum, olivary bodies, suprachiasmatic region, caudate nucleus, and orbital cortex. The striking feature was the extreme patchiness of the change. Small groups of cells showed Nissl degeneration, with or without eccentricity of the nucleus, vacuolation of the cytoplasm, and haziness or bursting of the cell margin, whereas cells only 100–200 μ away appeared perfectly normal. There was no spatial pattern of degeneration. Many investigators, including Langworthy (1930), have observed this extreme patchiness of cell degeneration.

Of the cause or causes of the changes seen at necropsy in the brain in deaths from lightning or electric shock Critchley (1934) says: "Probably the blood-vessels constitute the main routes for the passages of currents through the brain, and many of the changes found at autopsy are explicable on the basis of a primary vascular lesion." Certainly the changes are not in themselves specific for electrical death. Critchley says that changes due to current, to heat caused by it, and to toxæmia after burns or cerebral concussion would be difficult of differentiation one from the other. Langworthy (1930) states: "The abnormalities following the electric injury are characteristic for injured nerve-cells no matter what the inciting cause." Pietrusky (1926) considered most of the findings consistent with "internal suffocation." Lieut.-Colonel Albert Sachs has told us that his findings in the brains of heat-stroke victims have been broadly similar to ours.

SUMMARY

Two cases of fatal lightning stroke, together with temporary effects in two others, are described. The outstanding features of the fatal cases were hæmorrhages and necrosis in the pancreas and keraunographic marks on the exterior of the body.

Our thanks are due to Colonel J. A. Crawford, officer commanding Cambridge Hospital, Aldershot, for permission to publish these cases; Lieut.-Colonel Albert Sachs, R.A.M.C., A.D.P. Southern Command, for helpful advice and criticism, especially in connexion with the staining of the Nissl substance; Captain J. Sugden, R.A.M.C., for the photograph of the skin markings; and Mr. J. Napper, of the Welsh National School of Medicine, for the photomicrographs.

REFERENCES

Alexander, L. (1938) *J. industr. Hyg.* **20**, 191.
Charcot, J. M. (1890) *Wien. med. Wschr.* **40**, 9, 57, 104.
Critchley, M. (1932) *Brist. med. chir. J.* **49**, 285.
— (1934) *Lancet*, i, 68.
Dickson, W. E. (1947) *J. Path. Bact.* **59**, 3, 359.
Hopkins, A. E. (1924) *Anat. Rec.* **28**, 157.
Jaffé, R. H. (1928) *Arch. Path.* **5**, 837.
Jellinek, S. (1932a) *Wien. klin. Wschr.* **45**, 37.
— (1932b) Elektrische Verletzungen. Leipzig.
Kawamura (1921) *Virchows Arch.* **231**, 570.
Lancet (1944) ii, 446.
Lancet (1946) i, 351.

Continued at foot of next column

TUBERCULOUS ABSCESS AT THE SITE OF PENICILLIN INJECTIONS

G. B. FORBES, M.B. Aberd.
ASSISTANT PATHOLOGIST

F. G. St. CLAIR STRANGE, F.R.C.S.
ORTHOPÆDIC SURGEON
KENT AND CANTERBURY HOSPITAL

THE formation of an intramuscular tuberculous abscess subsequent to, and at the site of, injection of penicillin has been reported previously. The case of Ebrill and Elek [1] was that of a boy with a staphylococcal axillary abscess for which penicillin was given by intramuscular injection into both thighs. He was readmitted to hospital three months later with an abscess of the left thigh which proved on bacteriological examination to be tuberculous. Hindenach's [2] case was that of a small boy with tuberculous abscesses of both thighs following the injection of penicillin in those sites, the primary lesion for which penicillin was given being a cervical abscess.

We believe that this unfortunate complication of penicillin therapy is not so rare as the paucity of published reports suggests. We have recently seen another case, and we know of two more. We therefore wish to urge a more complete bacteriological investigation of "sterile" pus from penicillin-treated patients.

CASE-RECORD

A male cashier, aged 29, was admitted to hospital on Dec. 10, 1947, with a history of pyæmic arthritis of the right hip-joint at the age of 15. He had been more or less continuously under treatment since that time, and had had local symptoms in the right ulna (1943) and the right third metacarpal (1934 and 1940), which had, however, both subsided without operation in two or three weeks. Details of these incidents are not known, but it is thought that they may have been low-grade pyæmic phenomena.

On the present occasion he had pain in the right buttock, and an acute abscess was found there. The hip was clinically and radiologically ankylosed in fair position, with 4 in. of combined shortening. Since the abscess was deeply situated, the patient was given systemic penicillin, of which he received 10·5 mega units, involving some 42 injections into the lateral aspect of the left thigh, over a period of three weeks. The abscess subsided without sinus formation, and the patient was discharged on Jan. 6, 1948. He was seen again as an outpatient two weeks after his discharge and was allowed to return to work.

On Feb. 2, 1948, he attended the outpatient clinic with three days' history of a swelling in the left leg. A diffuse swelling was found on the outer side of the middle of the left thigh; this was soft, fluctuant, and fairly tender, but not red. There was no tenderness in the inguinal lymph-nodes on this side, which were mobile and only just palpable.

The patient was readmitted on Feb. 23, and the abscess, which had formed at the site of the penicillin injections, was aspirated. The pus contained acid-fast bacilli morphologically typical of tubercle bacilli, and a heavy pure growth of *M. tuberculosis* (human) was obtained on Lowenstein-Jensen medium. Routine culture on ordinary media gave no growth. A guineapig inoculated with the pus died of generalised abdominal tuberculosis five weeks after the injection. A Mantoux test was done only after the development of the abscess, and, as might be expected, was strongly positive. The erythrocyte-sedimentation rate at this stage was 20 mm.

1. Ebrill, D., Elek, S. D. *Lancet*, 1946, ii, 379.
2. Hindenach, J. C. R. *Proc. R. Soc. Med.* 1947, **40**, 161.

MAJOR LYNCH, MAJOR SHORTHOUSE: REFERENCES—*cont.*

Langworthy, O. R. (1930) *Bull. Johns Hopk. Hosp.* **47**, 11.
Leys, D. (1942) *Edinb. med. J.* **49**, 657.
Loewenstein, K., Mendel, K. (1932) *Dtsch. Z. Nervenheilk.* **125**, 211.
MacLachlan, W. (1930) *J. industr. Hyg.* **12**, 291.
MacMahon, H. E. (1929) *Amer. J. Path.* **5**, 333.
Panse, F. (1925) *Mschr. Psych. Neurol.* **59**, 323.
Pietrusky, F. (1926) *Dtsch. Z. ges. gerichtl. Med.* **6**, 535.
Sestier, A. D. F. (1866) De la foudre. Paris.
Spencer, H. A. (1932) Lightning, Lightning-stroke and its Treatment. London.
Spitzka, E. A., Radasch, H. E. (1912) *Amer. J. med. Sci.* **144**, 341.
Urquhart, R. W. I. (1927) *J. industr. Hyg.* **9**, 140.
Werner, A. H. (1923) *N.Y. med. J.* **118**, 498.

Digitized by Google

in 1 hour (Wintrobe). There was no clinical or radiological evidence of tuberculosis in chest or abdomen; gastric lavage and examination of fæces for tubercle bacilli proved negative.

A small sinus developed at one of the punctures, but this healed within two weeks, and the patient was again discharged on May 8. Five months later there was no recurrence of discharge and no evidence of an abscess, though there was still a little residual thickening at the site.

DISCUSSION

This patient's case-report before we first saw him in December, 1947, is incomplete, but the available evidence points to a primary diagnosis of acute osteomyelitis of the upper end of the right femur at the age of 15, with spread to the right hip-joint, producing a septic arthritis. A series of local exacerbations and metastatic abscesses then followed, and latterly responded well to penicillin therapy without the need for surgical intervention. Though bacteriological proof is lacking, it seems probable that the causal micro-organism was a penicillin-sensitive staphylococcus. The clinical and radiological findings and the course of the disease are much more in keeping with a chronic staphylococcal infection than with a tuberculous one, though it is impossible to be certain that the original hip lesion was not tuberculous. The postpenicillin abscess was, so far as we can ascertain, the first and only manifestation of tuberculosis.

Ebrill and Elek [1] contended that the abscess in their case was a primary tuberculous one, probably due to the introduction of virulent tubercle bacilli with the penicillin solution. They based this view on the elimination of other possible sources of infection. They emphasised the absence of any evidence of tuberculosis in their patient other than the postpenicillin abscess. We too have been unable to detect a focus of tuberculosis elsewhere in the body of our patient, but we none the less favour Hounslow's [3] view that such abscesses are most likely to be postprimary—i.e., occurring in a person already the subject of tuberculosis and harbouring a cryptic primary focus. The primary lesion may be in a part of the body where its detection is difficult—e.g., the alimentary tract—or, if it is in a more accessible position, the primary lesion may be so minute as to escape detection though still capable of causing a transient bacillæmia. Devitalised tissues, or a small hæmatoma at the site of penicillin injection, would act as a favourable soil for the lodgement and multiplication of tubercle bacilli carried by the blood-stream, a course of events similar to that believed to occur in tuberculosis of bones and joints following injury. The fact that the abscesses in Hindenach's case were situated in both thighs further supports the hæmatogenous theory.

The possibility of infection by direct inoculation of tubercle bacilli, either in the penicillin solution or in the apparatus used to inject it, is unlikely but cannot be entirely dismissed. It is the practice in this hospital (as in most) to inject penicillin with syringes reserved solely for this purpose; the use of penicillin syringes for aspiration is strictly forbidden. At the same time there may be a tendency among nurses and sisters to exercise less than usual care in the sterilisation and handling of penicillin syringes in the mistaken belief that penicillin is a potent universal antiseptic. For this reason we endorse the plea of Ebrill and Elek for a more rigid aseptic technique in the administration of penicillin, even though we believe that the condition described here is usually the result of a hæmatogenous infection.

SUMMARY

A case of tuberculous abscess developing deeply in the thigh at the site of previous penicillin injections is described. Reasons are given for supposing that the infection was hæmatogenous.

3. Hounslow, A. G. *Lancet*, 1946, ii, 617.

LONG-ACTING PREPARATION OF TESTOSTERONE

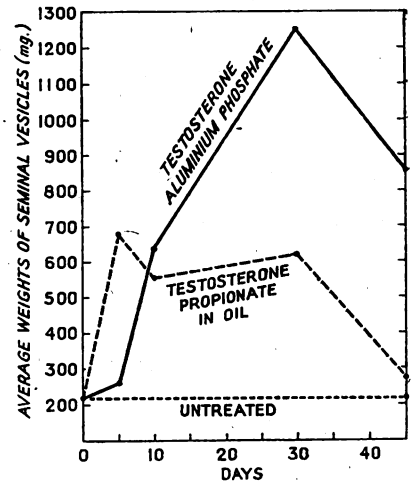
E. CARLINFANTI F. D'ALÒ L. CUTOLO

From the Istituto Sieroterapico Italiano, Naples

THE therapeutic efficiency of hormones is much influenced by the route and form of administration. High concentrations in the blood and tissues are sometimes necessary, and these are most easily attained by using the intravenous route. In our laboratories a water-soluble derivative of testosterone has been synthesised which is well tolerated when injected intravenously, even in large amounts, and has given satisfactory results in certain morbid conditions, such as polycystic mastitis.

On the other hand, for the protracted maintenance of a physiologically useful concentration in the blood repeated inoculations are impracticable; and means had therefore to be found for effecting continuous slow absorption from the site of injection. The maximum of utilisation is not easily attained, since excessive concentrations in the blood are rapidly corrected by renal excretion and by destruction in the liver.

This type of problem has been partially solved in the field of insulin therapy, but no easy solution has been found to date in the use of synthetic hormones. One method of overcoming the difficulty is the subcutaneous implantation of compressed pellets from which the hormones are slowly absorbed. This method has two serious disadvantages: surgical operation is involved, and intolerance of the drug by the tissues often leads to imperfect healing and expulsion of the pellet. Efforts have therefore been made to find alternative means of obtaining the desired depot effect with a less radical procedure. The usual aqueous suspensions of the hormone are unsuitable because they are composed of crystals of various sizes, the largest of which can be injected only through a coarse needle.



The use of insoluble aluminium salts as adjuvants in vaccine prophylactics suggested to us a way of preparing testosterone which has a very protracted action, can be administered with ordinary fine needles, and causes no untoward reactions. This new preparation also has the advantage that it is always ready for use and remains stable for a long time. We are convinced that the same method could be applied equally successfully to other hormones, both synthetic and natural.

PREPARATION

To a solution of 1 g. of crystalline testosterone (melting-point 154·5°C) in 10 ml. of 96% ethyl alcohol is slowly added, with constant stirring, 20 ml. of an aqueous suspension of aluminium phosphate 7 mg. per ml. The mixture is allowed to sediment, and the supernatant fluid is decanted off. The residue is made up to 40 ml. with saline solution.

In this work we used pure testosterone and not the propionate ester, since the former is less irritant.

Digitized by Google

AVERAGE WEIGHTS OF SEMINAL VESICLES OF CASTRATED GUINEAPIGS AFTER ONE INJECTION OF TESTOSTERONE 0·25 MG. PER G. OF BODY-WEIGHT

Time after injection (days)	Testosterone propionate		Testosterone aluminium phosphate	
	No. of guineapigs	Average weight of seminal vesicles (mg.)	No. of guineapigs	Average weight of seminal vesicles (mg.)
3	2	683	2	262
7–8	7	566	4	638
30	4	620	4	1255
45	6	277	2	859

In 24 guineapigs the average weight of the seminal vesicles was 218 mg.

Aluminium phosphate as used by Holt[1] in the preparation of his diphtheria prophylactic (P.T.A.P.) was adopted by us because of its easy preparation and desired properties.

Experiments have been made on guineapigs, which, like rats, show atrophy of prostate, seminal vesicles, &c., after castration. We have taken advantage of the regenerating effect of the hormone on the atrophic vesicles resulting from castration. This regeneration rapidly regresses after the disappearance of the hormone from the body. In preliminary experiments we have observed that twenty days after castration the seminal vesicles of a 400 g. guineapig weigh on an average 218 mg. (24 guineapigs examined). Twenty days after castration a group of guineapigs were given a subcutaneous inoculation of 25 mg. per 100 g. of body-weight of testosterone propionate dissolved in oil, and another group received the same amount of pure testosterone adsorbed on to aluminium phosphate, administered in the same way. The effects of the two preparations on the weight of the seminal vesicles (see table and figure) show that one inoculation of the ester-in-oil leads to a rapid rise and fall in vesicle weight, whereas the new preparation produces a greater and longer-continued action, reaching a peak not earlier than thirty days after administration.

SUMMARY

A preparation of testosterone with depot action is described. It is stable and can be administered with a fine needle. It has the advantage of reducing the frequency of injections to one a month or less and obviates the need for surgical implantation of pellets.

A WHEEL-CHAIR

A. G. BRUCE POOLE
M.B. Edin.

THE wheel-chair described here has been built for a man with major disablement following infantile paralysis. No originality is claimed, but the special features it embodies may be of interest.

The chair has been made to fit a tall young man wearing a Forrester-Brown brace and callipers. His disablement amounts to a total loss of function of the muscles of both legs and of the right arm, with subtotal loss of function of those of the left upper arm and of the lower abdomen. He cannot walk, raise himself to the sitting position, move his body, or lift his left hand to his mouth; but he can use his left forearm and hand. The problem has been to design a chair in which he can remain all day for every purpose, even when travelling in a motor-car—i.e., a chair in which he can be self-supporting wherever he goes. At night a plaster shell is used.

In its evolution there have been three models, each built of a different material: wood, steel, and aluminium. Wood was cumbersome. Steel was satisfactory. The model in steel was in use for about six years; but it had some disadvantages compared with the present aluminium model (fig. 1).

The materials were as follows:

Material	*Description*	*Outside dimensions (in.)*	*Parts*
Aluminium	Channel	1·0 × 0·8125 × 0·0625	Frames
	Tube	0·048 × 0·648 and × 0·75	Supports and handle-bars
	Sheet	0·36 × 24 × 36	Coverings
		0·64 × 24 × 24	Gusset-plates and hinges
		0·125 × 24 × 24	
		0·25 × 24 × 24	
	Rod	Assorted	Nuts, &c.
	Rivets	1/8 diam. × 7/16 & 5/8	..
Steel	Sheet	1/16 & 1/8	Runners, &c.
	Tube		Back supports
	Bolts, &c.	Assorted	..
	Ball-races	..	..
Tin	Sheet	1/16	Hinge-lining
Wood	..	..	Block inserts
Leather or canvas	..	..	Linings

The aluminium is an alloy used in aircraft construction. Channel—i.e., U-shaped material—was selected for the framework, because it is easier to join and to support than tubing and is not particularly difficult to shape by bending. Apart from an adequately appointed workshop the only special pieces of apparatus required were bending-machines, which were made in the workshop.

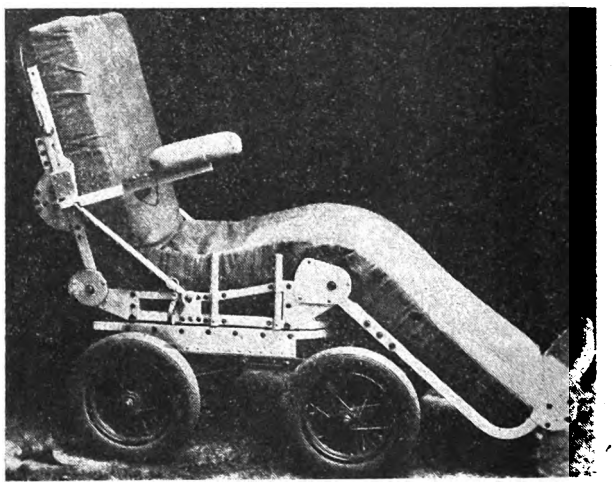


Fig. 1—The aluminium chair.

The foundations of the chair proper consist of three frames—back, seat, and leg—each constructed of channel bent to the required shape and joined at one place only by plate and rivets. The seat frame is linked to the back and leg frames by hinges which work on the principle of those used on hinged callipers. The hinges were specially designed, and each set varies slightly according to the requirements of the chair. They all contain stops to limit the movement at the required range and are lined with tin to prevent the aluminium from dragging. All the moving parts are fitted with ball-races to give ease of movement and to prevent wear. Each part was made separately as a unit, and the chair was assembled with bolts to allow of any unit being removed, should replacement be necessary. Without upholstery and fittings the chair consists of two main parts: the chassis with its wheels, and the chair proper.

THE WHEEL-CHASSIS

The chassis is made up of three separate parts: (1) axles, springs, and supporting structure of steel made

1. Holt, L. B. *Lancet*, 1947, i, 282.

Digitized by Google

Fig. 2—Transporting the chair.

from a cut down Richards chair; (2) Dunlop pneumatic 12 × 2 in. cycle-type wheels with ball-bearings as used on light barrows; and (3) a special aluminium and steel fitting designed for attachment of the chair. This special fitting consists essentially of runners with guides, grips, and fasteners, and is so placed over the axles that the chair is balanced when the back is up or down.

The chair is simply and rapidly attached. The base of the chair, on which are four small wheels, is placed on the runners, and as the chair is pushed home it is guided automatically into channel pieces that grip the front and rear transverse bars of the base. Once in position the chair is fixed by fasteners placed at the back of this fitting. The chair and wheel-chassis can then be lifted off the ground and the whole carried as one unit.

For travelling by car the wheel-chassis is detached and placed on the luggage grid, and the chair is accommodated on the floor of the car (fig. 2). A 10 H.P. saloon car with four doors is sufficiently commodious to take the chair after one of the front bucket-seats and the back seat have been removed. One passenger can still be carried in the back. As a refinement a floor-board is fitted.

THE CHAIR PROPER

Though the assembled chair proper may appear complicated, the back, seat, hinges, and the leg-rest are simple in design and construction.

The back consists of a single frame to which are bolted gusset-plates to hold a fixed handle-bar and to house the hinges of a movable one. The fixed bar for lifting is made of tube. The movable one for pushing is made of channel blocked with wood and covered with leather to make it pleasant to handle. The back is attached to the seat hinges and held in position by supports which work on the principle of one tube sliding within another, fixation in the desired position being effected by pin and slot. When the chair is pushed forward or pulled back, the main thrust is taken through these supports. In the sitting position they hold up the back at 25° from the vertical, but when the back is let down they are not in action, the back in this position being supported on the stops in the hinges. Thus, to lower the back, all that is necessary is to pull out the pins.

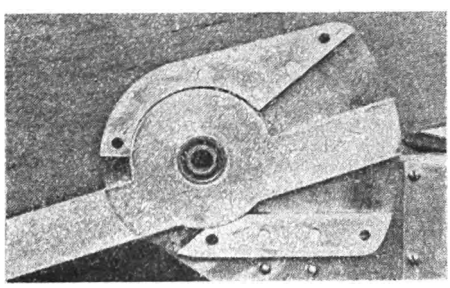


Fig. 3—Front hinge with cover-plate removed.

The seat in its initial stages of construction consists of a single frame; on this uprights are bolted which support an upper frame bent to conform roughly to the anatomical shape of the buttocks. Attachment of the front and rear hinges completes the seat piece as a unit.

The hinges are an important part of the chair. Each consists of two main parts: fixed, and movable. The fixed part is made of $^1/_8$ in. sheet and is bolted to the side of the seat frames and, because the corners are rounded, it is also bolted to the transverse portions of the frames; this is done by means of a plate rivetted at right-angles to the hinge. Such a method is an advantage in that it prevents sideplay. To give the rear hinges additional stability a transverse bar is fitted which also acts as an additional handle-bar for lifting. The movable part is made of $^1/_4$ in. sheet, a cover-plate enclosing it. The front hinge with its cover-plate removed to display the internal workings is shown in fig. 3.

The leg-rest consists of a single frame reinforced with cross-members, covered with thin sheet aluminium, and fitted with a handle-bar for lifting.

UPHOLSTERY AND FITTINGS

Leather is used to line the back and seat, though canvas is also satisfactory. Attachment is by lacing rather than stitching, so that tension can readily be adjusted. Any material is inclined to sag and to squeeze the buttocks and thighs. To prevent this happening, a bar of wood is placed transversely across the material to maintain the necessary tension in the required place. A Dunlop honeycombed rubber mattress measuring 6 ft. × 18 in. × 4 in. and weighing 15 lb. covers the back, seat, and leg-rest. In addition, small wedge-shaped rubber cushions are used to support the feet and to wedge them gently when they are in position.

Fig. 4—Table in use in low position.

The fittings are as follows:

(1) A head-rest, consisting of a light metal frame covered with canvas, is used when the back is down. For attachment it is fitted with prongs which slip into slots on the chair.

(2) A hinged splint is attached to the brace to support the left arm.

(3) An arm-rest, fitted to the chair to support the right arm, can be raised or lowered and swung round to the rear to be out of the way, and bears a pad sliding in a slotted groove to support the wrist and hand.

(4) A table has been specially designed, since the disabled person sits up leaning slightly back and cannot raise the left hand to the mouth unless the upper arm is supported. The height of the table and its proximity to the body are adjusted for writing or for meals by using a set of legs of the required length. The legs are of wood and are supported by metal tubes attached to the chair and fitting into slots under the table. The top is the width of the chair and has three leaves each of a different length linked by hinges so that the table can fold and fit closely to the body when used either in the low or the high position (fig. 4)

(5) A stand to hold a musical instrument, and another to hold music.

Digitized by Google

Before his disablement the young man played the clarinet. Loss of function of the right hand deprived him of this hobby; but as soon as he realised what could be achieved by aids he determined to try to play an instrument which requires the left hand only, and selected the French horn. A stand with many joints was then designed to hold and adjust it. He is now in demand by local amateur orchestras.

Being self-contained in his chair he is, for practical purposes, able to lead the life of an ordinary citizen. He has graduated at a university and has now taken his place in business.

DISCUSSION

The chair was designed from several years' experience in the daily use of a previous model in steel.

The main considerations were that the chair should be comfortable, easy to manipulate, easy to transport, and self-contained. Where there is wasting of muscles over an extensive area, pressure must be borne evenly over the whole of the affected parts. For this reason the seat, back, and leg-rest were designed, when covered with a honeycombed rubber mattress 4 in. thick, to conform roughly to the anatomical shape of the body, a fine degree of adjustment being possible by altering the tension of the lacing. Provided all wrinkles are removed from the clothing when the disabled person is placed in the chair, comfort is not disturbed when the back is lowered for change of position. The urinal is used with the back lowered; the bedpan with it raised. To place the bedpan in position, the technique is to lower the back, raise the buttocks, slip the bedpan into position, then raise the back, and cover the thighs with a carbon-impregnated cloth. Two attendants are required, though one can manage.

For ease of manipulation all the moving parts are fitted with ball-races. Without ball-races the moving parts soon wear out. Once wear sets in, with the amount of man-handling the chair is subjected to, the construction loses its stability. Ball-races are therefore not a refinement but essential. The design of the hinges and their method of fixation make the chair rigid, though there is some whip in the material. The chair weighs 31 lb.

Ease of transport has been achieved by designing a detachable wheel-chassis with a simple attaching device. There is no difficulty in loading the chair into a car, any passer-by in the street can be called on to give a hand. The wheel-chassis weighs 39 lb. The weight could be reduced slightly by fitting solid rubber tyres to the wheels; but the pneumatic-tyred wheels, though heavier, are a great boon, especially for cross-country work, and make the chair look as if it had been built for a disabled person rather than an invalid.

The chair is self-contained as regards fittings, such as writing-table, dining-table, head-rest, and arm-rest. These fittings are easy to carry and thus make it possible for the disabled person to take his place in society.

This chair has passed through its users' trials successfully and is giving satisfactory results. The cost of its construction is difficult to estimate, because it was not made in a commercial workshop, and each part was cut from raw material and shaped by hand. It took a long time to make, but its usefulness is an adequate reward for the time spent. The materials are not costly. In this article technical details have been purposely omitted, but I will be pleased to give them to anyone who may wish to construct a chair on similar lines.

I wish to thank my father, Major-General L. T. Poole, C.B., D.S.O., M.C., for his guidance, and Mr. B. N. H. Thornley, of the developments department of the Northern Aluminium Co. Ltd., for selecting the materials required.

Medical Societies

EDINBURGH OBSTETRICAL SOCIETY

Incoördinate Uterine Action

AT a meeting of this society on Feb. 9, with Dr. E. C. FAHMY, the president, in the chair, a paper on incoördinate uterine action in labour was presented by Prof. T. N. A. JEFFCOATE (Liverpool).

Professor Jeffcoate criticised the use of the term "uterine inertia" on the score that incoördinate uterine action was often associated with high muscle-tone, especially in the middle and lower zones, or with spasmodic violent contractions, or with a constriction ring. The clinical picture was one of prolonged labour with slow dilatation of the cervix, despite the presence of strong uterine contractions and the absence of gross disproportion. Pain, which was unusually distressing, was felt predominantly in the back; sometimes, when it assumed a down-bearing nature before full dilatation of the cervix, it appeared to arise through spasm of the lower bowel. All degrees of incoördinate action might be found; and it was particularly liable to occur in the presence of disproportion.

Of 101 cases observed in Liverpool, 62 were seen in private practice and 39 in hospital. The incidence in hospital cases was 0·6%; the condition was seen more often in private practice, but it was not possible to work out any very reliable figures of its incidence here. The disorder was almost entirely confined to primigravid patients, but the ætiological influence of advancing age had been exaggerated. Premature rupture of the membranes did not appear to be a direct cause, since this occurred in only 22 cases, whereas in 56 the disordered action of the uterus was recognised prior to rupture. Indeed, even when the membranes were unruptured the uterine disturbance was sometimes enough to cause embarrassment of the fœtus. The significance of the occipitoposterior position as a cause of incoördinate action had been confirmed, and delayed engagement of the head in occipito-anterior position was noted often.

The maternal and fœtal dangers of this condition had diminished with the introduction of chemotherapy, better general care of the parturient, caution over anæsthesia, and readiness to resort to cæsarean section late in labour. Nevertheless, the dangers were still present, although in the two series no mothers died and the fœtal loss by stillbirth and neonatal death was only 12%. Professor Jeffcoate estimated that but for cæsarean section the fœtal mortality would have been in the neighbourhood of 50%.

A further series of cases had been investigated in respect of remote prognosis. Of 140 severe but non-fatal cases requiring cæsarean section or forceps delivery during the years 1936–46, 91 had been traced. As a result of their experiences more than one-third of these patients decided to avoid further pregnancy; only half had further children. As regards this voluntary infertility, there was little difference between the cæsarean-section group and that in which forceps had been used; but all the women who had lost their first children tried subsequently to conceive, while contraception was practised only by those who had a living child. A few women embarked on further pregnancy only when promised that delivery would be by elective cæsarean section. In general terms the follow-up showed that in a large proportion of cases the behaviour of the uterus was much more efficient in the second labour, and that whereas cæsarean section might be necessary in the first labour there was a good chance of vaginal delivery in the second. The ease of the second delivery appeared to be to some extent proportional to the stage of dilatation reached by the cervix at the first labour. When full dilatation had been attained, even if the baby had been delivered dead and with difficulty, the second labour was usually easy. Caution was therefore necessary in advising elective cæsarean section solely because of a "bad obstetric history."

In the control of disordered uterine action, the administration of analgesics and antispasmodics, particularly morphine and pethidine, remained the chief line of attack. Professor Jeffcoate reported generally dis-

Digitized by Google

appointing results with intravenous magnesium sulphate, trinitroglycerin, and œstrogens. After intravenous administration of dilute solutions of oxytocin in glucose-saline, as recently advocated by Theobald and others, two of his patients had suffered most severe pain without any change in the nature of the contractions, which remained incoördinate. In each of 11 cases tetraethyl-ammonium chloride had appeared to produce a strong and sustained uterine contraction, sufficient in 1 case to cause alarm for the fœtus. When this contraction had passed off, the patients experienced more frequent, and apparently stronger, uterine contractions for up to one hour; but again there was no evidence of alteration in the nature of the contractions, and 2 cases of constriction ring persisted.

Professor Jeffcoate criticised the contention that fear and emotional tension were important in the ætiology of incoördinate uterine action; for this condition did not recur in deliveries after the first, even when the first had been sufficient to daunt the stoutest heart. He thought that an unnatural resistance of the soft tissues of the lower part of the uterus might be more important than neuromuscularim balance resulting from fear. In conclusion he classified inefficient uterine action under the headings of (1) inertia proper, (2) incoördinate uterine action, and (3) cervical dystocia.

Reviews of Books

Critical Studies in Neurology

F. M. R. WALSHE, M.D., F.R.C.P., F.R.S., physician to University College Hospital and to the National Hospital for Nervous Diseases, Queen Square. Edinburgh: E. & S. Livingstone. 1948. Pp. 256. 15*s*.

OF late years research in medicine has come to be regarded as almost synonymous with the discovery of new facts. As Dr. Walshe points out in the foreword of this book, the climate of opinion does not favour the critical. The facts, however, need interpretation, and, if this is not consciously sought, an erroneous interpretation is often unconsciously assumed. Thus the distinction between critical and creative research is an artificial one, as was well shown by the work of Hughlings Jackson, in whose discoveries it is impossible to separate the rôle of reflection from that of observation. Hence, in his new book Dr. Walshe is employing the Jacksonian method. All but one of these essays have previously been published in *Brain*, but it is to be hoped that, gathered thus into one volume, they will reach a larger public. The first, on the anatomy and physiology of cutaneous sensibility, contains a criticism of the views of Head and Rivers and an account of recent work chiefly on the peripheral organisation of sensation. This is followed by a study of the motor cortex and the pyramidal tract, in which Dr. Walshe discusses the attempt to delimit the motor cortex in terms of its cellular structure and reasserts his objection to Fulton's view that there is a functional difference between area 4 and area 6. The third essay, on the mode of representation of movements in the motor cortex, is a study of the inferences which can be drawn from Jacksonian convulsions concerning the functional organisation of the motor cortex. Dr. Walshe believes that movements are represented not by a mosaic of isolable points but "on a plan of wide and overlapping fields, each of which has a focus wherein the movements of a given motile part are mainly, but not exclusively, localised." Then follow two shorter papers in which the same theme is developed, and the last chapter is on the integration of medicine and is a discussion of those philosophical principles which have found a practical expression in the rest of the book. Differentiation and integration in the development and activities of the organism are paralleled by observation and interpretation in the sphere of the mind. These are the systole and diastole of medical research—the opposites without which, as Blake says, there is no progression. This is Dr. Walshe's salutary message for our times, and here he is both preacher and practitioner.

Detailed Atlas of the Head and Neck

RAYMOND C. TRUEX, M.S., PH.D., associate professor of anatomy, College of Physicians and Surgeons, Columbia University, New York; CARL E. KELLNER, artist in the department of anatomy of the college. New York and London: Oxford University Press. 1948. Pp. 162. 75*s*.

THE most valuable atlases of anatomy have usually resulted from the coöperation of anatomists and artists. Such an association of Professor Truex with the artist Carl E. Kellner has been fully justified by the production of this accurate and attractive atlas of the anatomy of the head and neck. All the drawings in the first part of the book are from original dissections, and are notable for their clearness and their exact portrayal of successive stages in the dissection of particular regions. Outstanding features are the representation of the anatomy of the junctional regions of the neck with arm and thorax, and the instructive approaches to the dissection of various other regions (such as that through the middle cranial fossa and petrous temporal bone into the infra-temporal region). The second section contains some excellent drawings of skeletal structures. Finally, a series of coronal and transverse sections display in fine detail the topographical relations of structures in the neck and cranium. The large size of most of the drawings, together with a judicious use of colour for vessels, nerves, and (in the skull) separate bones and muscle attachments, make the various structures pleasingly distinct and favour the rapid comprehension of relationships. This atlas will be welcomed by teachers; it will also be of real value to the student for reference, and to the surgeon who wishes to review quickly the approach to cervical or cranial structures.

Anæsthesia for the Poor Risk

W. W. MUSHIN, M.B., D.A., director, department of anæsthetics, Welsh National School of Medicine, Cardiff. Oxford: Blackwell Scientific Publications. 1948. Pp. 65. 7*s*. 6*d*.

THIS is an excellent little book. Lightly written, it allows the reader to survey a wide range of anæsthetics pleasantly in one evening by the fireside. These one-page essays, the first of which gives its name to the book, teach nothing of technique, but much of philosophy, and even more of common sense. It could more helpfully have been entitled "The Intelligent Doctor's Guide to Anæsthetics"; and every surgeon would be the better for reading it.

Tuberculosis

A Discussion of Phthisisgenesis, Immunology, Pathologic Physiology, Diagnosis, and Treatment. FRANCIS MARION POTTENGER, A.M., M.D., LL.D., F.A.C.P., emeritus professor of medicine, University of Southern California; director of the Pottenger Sanatorium and Clinic for Diseases of the Chest. London: Henry Kimpton. 1948. Pp. 597. 60*s*.

THE key to Dr. Pottenger's book is his confession that fifty years of medical practice have left him with very little phthisiophobia. He looks on tuberculosis as a disease which is only mildly infectious and which offers the greatest possible opportunity for eradication. The primary infection is to him a vaccination, and, were it not for the fact that it sometimes provides a focus from which future metastases arise, it would be a desirable form of immunisation. With these basic conceptions in his mind and long practical experience to draw on, he sets out to portray tuberculosis as a sometimes destructive but more often a localising and healing disease with a hopeful prognosis. In fact he has a sturdy faith in the resistance of the patient, in the great value of the good sanatorium, and in the skill and guidance of a wise physician—sometimes reinforced by a surgeon. In all this the book is essentially clinical in its outlook, with the emphasis on the good vintage of the ancient régime.

There are separate chapters on each of the classical methods of examination—inspection, palpation, percussion, and auscultation—and only the same allowance (and a short one at that) for radiology. In discussing the search for the tubercle bacillus, Dr. Pottenger rightly emphasises the value of concentration methods of examining sputum; but newer methods such as gastric lavage and laryngeal swab cultivation are not stressed. Morbid anatomy receives less attention

Digitized by Google

perhaps than it deserves as a background of the disease, though there are useful chapters on the primary complex and reinfection and a valuable series of no less than five on complications. The triad of open air, rest, and a well-selected diet is fully honoured, and pulmonary tuberculosis in childhood, so often relegated to an insignificant section in textbooks, receives due attention. New ground is broken in two chapters on the visceral neurology of tuberculosis in which he discusses the action of various reflexes in phthisis. Dr. Pottenger believes that tuberculin therapy plays an important part in treatment—after using it for half a century he has seen only the happiest results—and he expands his views to the length of a whole chapter; but he gives little notice to modern chemotherapy.

He takes his stand indeed on the diagnostic and therapeutic methods which have well and truly stood the test of his long experience; but he leaves the reader wondering whether, in these days of extreme specialisation, a general textbook on pulmonary tuberculosis can really be based on the experience of a single writer.

The Modern Management of Gastric and Duodenal Ulcer

Editor: F. CROXON DELLER, M.D. Edinburgh: E. & S. Livingstone. 1948. Pp. 227. 20*s*.

Dr. Deller has presented a well-balanced description and review of the treatment of gastric cases. It is refreshing to follow his broad approach to the management of the patient as well as to the management of his local disease. Diagnosis from the clinical aspect is well considered and there is a good chapter on radiology with careful description and discussion of the variations in the appearances of gastric lesions. The chapter on the Decision on Treatment is particularly good, and the detailed instructions for treatment will be useful to the general practitioner in his everyday work. Perhaps too much of the book is given over to minute description and illustration of technical points in surgical operations on the stomach, which are fully covered by other works. Instead, more attention might have been given to modern gastroscopy and the wide bearing it has on diagnosis and choice of treatment. But these are minor criticisms of a well-written and useful work.

Review of Plastic and Reconstructive Surgery

EARL CALVIN PADGETT, M.D., professor of clinical surgery, University of Kansas; KATHRYN LYLE STEPHENSON, M.D., instructor in plastic surgery, Tulane University, Louisiana. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 945. 126*s*.

THIS is probably the most ambitious work on the surgery of repair yet attempted. The senior author—well known for his invention of the dermatome, or calibrated skin-cutting machine—has tried to unite in one volume principles and practice of repair in all tissues of the body. His untimely death in 1948, before the manuscript was completed, left Dr. Stephenson with a heavy responsibility which she has ably fulfilled.

It is hard to write a comprehensive work on plastic surgery which will satisfy plastic surgeons on the one hand and general surgeons on the other: hence this is a notable achievement. The general principles of repair are covered, and the transplantation of all tissues of the body fully considered. The excellent chapters on trauma include one on burns to which the senior author contributed much during his lifetime. Congenital and acquired defects are fully dealt with, and the reconstructive surgery of special regions and conditions is then discussed in great detail, methods being illustrated by good clear line or wash drawings. Some of the photographs of results are not up to standard and should be replaced. Much work generally regarded as belonging to other fields (thoracic, gastric, orthopædic) might with advantage have been omitted: chapter XIX is almost entirely concerned with operations better presented in many standard orthopædic textbooks, and the same criticism holds for the sections on œsophago-gastrostomy and so-called plastic operations on the kidney pelvis. No doubt this could be remedied in the future editions through which this book is certainly destined to pass.

Teach Yourself Physiology (London: English Universities Press. 1948. Pp. 207. 4*s*. 6*d*.).—Mr. David Le Vay, F.R.C.S., gives us a good presentation of physiology at an elementary level along conventional lines. It is brief, business-like, and attractively illustrated, and designed as a useful rather than an inspiring introduction. It can be recommended to those who have practical facilities, or whose work provides them with experience of the human body.

Thomson-Walker's Genito-Urinary Surgery (3rd ed. London: Cassell. 1948. Pp. 956. 60*s*.).—Mr. Kenneth Walker has undertaken an onerous task in bringing up to date this old favourite. He has certainly succeeded in preserving the personal character of the book, perhaps at the expense of retaining material which must now be considered obsolescent. The fact that a third edition of the work has been called for is evidence of its popularity.

Refraction of the Eye (3rd ed. London: Henry Kimpton. 1948. Pp. 287. 27*s*. 6*d*.).—There have been no radical changes in this American book. Indeed it is not easy to find points of difference from the previous edition. Prof. Alfred Cowan describes in detail the properties of lenses and mirrors and the optical properties of the eye, the methods of prescribing glasses from the plane mirror to the ophthalmometer, the testing of muscle balance, and the uses of contact and telescopic lenses. The exposition is clear and concise, and the advice on spectacle-wearing is sound.

Introduction to Public Health (Bristol: John Wright & Sons. 1949. Pp. 271. 15*s*.).—Dr. E. W. Caryl Thomas's little volume is suitable for junior medical students, health visitors, and others working in public-health departments. It is too elementary to be of service to medical graduates who think of entering the public-health service, though they will find interest in the first two chapters. The chapter on communicable diseases contains little outside the curriculum of a pass examination in general medicine, and one or two statements—especially about the salmonellæ—are open to question. We could have wished that the chapter on National Health Insurance had been replaced by one on the National Health Service Act.

A Shetland Parish Doctor (Lerwick: T. & J. Manson. 1948. Pp. 136. 10*s*. 6*d*.).—Dr. H. P. Taylor's homely story of 45 years' work and play in the Shetlands proves him to have been a man of many parts. His excellent water-colours—the more remarkable since we are told they were painted late in life—show him to have had considerable talent in art as well as medicine. The rugged simple life of the islanders is portrayed as only a man who has lived and worked among them in such intimate association could do it. The very human stories, often full of humour, make good reading. The one of the old lady who noted the date of an observation on her calendar and was thereby able to inform the doctor of the parentage of a child born out of wedlock is a good example. The book has been produced in the Shetlands and bears the stamp of that self-reliance that one attributes to the inhabitants.

Diseases of the Nose and Throat (5th ed. London: Cassell. 1948. Pp. 1004. 70*s*.).—The late Sir St Clair Thomson was engaged on a comprehensive revision of his book when he died early in 1943, and his work has been continued and completed by Mr. V. E. Negus. The result is a well-produced and informative textbook, elegantly written. The sequence of chapters has been recast, out-of-date text and illustrations have been eliminated, and some sections have been completely rewritten. Full weight is given to chemotherapy. The importance of allergy in nasal disease is emphasised, but the fact that it is common in children (in whom it may be confused with sinusitis) is perhaps not sufficiently accentuated. The use of local anæsthesia alone or combined with thiopentone is not recommended in laryngofissure or laryngectomy, and the extended skin incisions of Gluck and Sorensen are preferred to a single midline incision. A number of other operative steps reveal a conservative outlook, probably desirable in a work of this nature. The book gives a careful account of all the diseases encountered in this region, the commoner conditions getting most space; and the treatment advised follows orthodox lines. Most of the illustrations are good and well chosen.

Digitized by Google

THE LANCET

LONDON: SATURDAY, MARCH 19, 1949

Specialists' Salaries

THE long-awaited "proposed terms and conditions of service of hospital medical and dental staff" have now been released; but, as the title of the memorandum shows, they are still provisional, and they are being published in order that the Joint Committee of Consultants and Specialists may learn the views of those affected. Whatever criticism of details may be offered, the profession's first reaction will be to acknowledge that the new arrangements constitute a generous and beneficent revolution in the financial status of its junior members. Residents will no longer be expected to work for several years for their board alone, or a little pocket-money in addition, and the "trainee specialist," as he is now to be called, will no longer have to depend on private means, coaching, or hack work during his early struggling years. The tough survivors of that process of financial selection may pretend that it was good for them: it is surely better for the nation that the entry to the higher levels of the profession should be widely open to talent, and also that intelligence should be able to afford to marry young. Before we begin to grumble, let us also recognise that the scale of remuneration as a whole is generous. Who would have predicted that a Socialist Government would have been prepared to pay specialists up to £2750 a year for all, and up to £5250 for those of special distinction? In fact the payments to trainee specialists may be initially too generous. For it is proposed to pay these doctors one year after registration over £200 a year more than their junior house-officer colleagues at the same period, and this may have the undesirable effect of encouraging too early specialisation.

The grades of junior and senior hospital medical officer are somewhat negatively defined as well as cumbersomely described. In many types of hospital there are doctors who will come into these categories, but it will not always be true to say that they are not specialists; in which case the establishment will include specialists "who are not of staff specialist status"—for example, many of the medical officers of mental hospitals. Large general hospitals, especially teaching hospitals, need many doctors of this type to do much responsible routine work in the psychiatric, ophthalmic, genito-urinary, venereal, and dermatological outpatient departments, and some of them have specialist status on the staffs of other hospitals. Is it the post or the practitioner that is to be graded? If the former, the anomaly will arise that a doctor is a specialist in one hospital and a hospital medical officer in another. If, on the other hand, the individual is graded, some hospitals will find their specialist staff enlarged by the inclusion of doctors whom they have previously classified as clinical assistants.

Last week's *New Statesman and Nation* contained an open letter to the Minister of Health reproaching him for his preferential treatment of the part-time as compared with the whole-time specialist. The part-timer, it alleges, is prone to neglect his work or to accept pay for sessions he does not attend, or is too anxious to amass sessions now that he is to be paid for them. Yet he is to be paid extra for domiciliary visits and allowed travelling expenses, and income-tax allowances under Schedule D, which are denied to the whole-timer. Perhaps the horns and tails of the part-timers are not so obvious, nor the haloes of the whole-timers quite so bright, as the writer implies. Nevertheless it seems to be true that the proposed terms favour the part-timer. Since he may earn up to $9^1/_2$ elevenths of a whole-time salary, in addition to his fees for domiciliary visits and the various allowances already mentioned, he may well be better off than the whole-timer and still have the right to practise privately. The source of this anomaly is that the Minister's policy in respect of hospital staffing has been one of laissez-faire. Since the balance between whole-time and part-time work in the service has been left to depend on individual choice, the Minister can only wait and see what happens and pay accordingly. The alternative is to decide in advance the ratio most suitable for the service, and regulate the supply of whole-timers and part-timers by varying the financial attractions of the two branches. This may well be impossible at the moment, at least for the country as a whole; but there is much to be said for encouraging regional boards to make local experiments which in time would yield the data on which more far-reaching decisions could be based. Meanwhile there seems no reason to deny the whole-timer his income-tax allowances on books and journals, and it might be wise to reduce slightly the maximum number of sessions which the part-timer is allowed to undertake. It should be noted that whole-timer and part-timer alike are entitled to additional remuneration for such duties as lecturing to nurses, and that both will be paid (by university or medical school) for whatever teaching of medical students and postgraduates they may undertake.

The proposed terms of remuneration must be seen against the background of the cuts in the budgets of the regional boards and the boards of teaching hospitals. Salaries cannot be cut, and there will, therefore, be a tendency to economise by reducing the number of specialists to be paid. Any reduction, on grounds of economy, in the number of trainee specialists would be short-sighted, and the growing demands on the hospital services show that we cannot do with fewer trained men and women. We can only, by better organisation, make the most economical use of those available.

Perhaps the most difficult financial problem that the profession has to face is the allocation of awards for special distinction. Here again we must recognise that the Government has shown both generosity and breadth of vision. The principle of incentives and rewards has been accepted with the general agreement of the profession. To detach the rewards from age and length of service was an act of imagination and perhaps daring. But (many are saying) has not the awards committee been set an impossible task? The answer is that the task will become possible only if

Digitized by Google

we frankly recognise that it is impossible. Distinction is incapable of quantitative measurement: it is a matter of opinion, about which one group of men will differ from another group equally painstaking and fair-minded. It follows that there must always be some recipients who might fairly claim a higher award than they will actually receive. If we recognise this at the outset it may smooth the path of the awards committee; and those who are disappointed can at least console themselves with the thought that after deduction of income-tax and surtax the differences between the awards are by no means as great as they look.

Names for Blood-cells

TODAY most British clinicians and pathologists use the same names for the various cells found in the blood and bone-marrow. Even when the names are not quite the same, the plan of nomenclature is a standard one: for instance some trace the normal development of the red blood-cells from a primitive pro-erythroblast through a series of "normoblasts" of varying maturity; others reserve "normoblast" for the latest stage before the cell loses its nucleus, and use "erythroblast" for the earlier stages. It is agreed that the megaloblasts are a pathological form of developing red blood-cell occurring only in the group of diseases characterised by absence of the anti-anæmic liver principle, or interference with its function. It is agreed that granular leucocytes, lymphocytes, monocytes, plasma cells, and megakaryocytes have separate lines of development from a primitive "blast" stage, through various intermediate developing and distinguishable types to the mature cell. It is also recognised that the bone-marrow contains a very primitive cell—the hæmocytoblast—that probably represents the earliest stage of the red-cell series, the granular leucocytes, the lymphocytes, and the monocytes.

This very considerable measure of agreement has been reached almost imperceptibly in the course of the past ten years. Fifteen years ago the British schools were still talking about the "megaloblast" as the mother cell for all red cells; plasma cells were still thought to be altered lymphocytes; and BARTA's work on the stages of development of the megakaryocytes had gone unrecognised. We do not now intend to describe the history of these changes; they have been brought to the notice of our readers in successive editorial articles in these columns. The stimulus to a more rational nomenclature for blood and bone-marrow cells has come mainly from studies of the sternal marrow, and the fully developed result of such studies can be seen in ISRAËLS's new atlas.[1] Our present nomenclature can be claimed to be more rational because it is based on ideas that have given us a much clearer view of the pathology—both anatomical and functional—and the treatment of many diseases of blood formation.

A system of nomenclature like the one we have outlined is now accepted in all Western Europe, in most of the British Commonwealth, and in South America. To the United States it spread more slowly. Most difficulty arose there over the conception of the megaloblast as a separate pathological series, because the ideas that the megaloblast was the primitive precursor of all red cells, and that in pernicious anæmia red-cell development was "arrested" at the megaloblast stage, had originated in American schools. Later publications from American schools and hospitals, particularly in the Eastern States, showed that the European system was being adopted, and recently a big impetus has been given to the recognition of a "normoblast-megaloblast" type of nomenclature by the demonstration that folic acid, and now vitamin B_{12}, are active only in those patients whose bone-marrow shows megaloblastic erythropoiesis—in the European sense of the term. But, even last year, some American textbooks were published that showed no recognition of these changes in nomenclature, and it was clear that, in the U.S.A. especially, many workers did not accept, or were unfamiliar with, these systems.

It was in these circumstances that the American Society of Clinical Pathologists and the American Medical Association set up a committee under the chairmanship of Dr. E. E. OSGOOD to consider nomenclature and to make recommendations that could be accepted by all and used as a standard—allowing for language variation, perhaps an international standard. The first report, on the leucocytic series, was published last May[2]: it distinguished a "progranulocyte" that nobody had needed before, and no very clear reasons were given for this separation; the spelling of "plasmablast" was oddly preferred to "plasmoblast"; but apart from these minor points, the proposals were generally acceptable. The proposals for the red-cell series were circulated later and have now appeared in print.[3 4] Here the committee thought it necessary to abandon the classical names: their reasons were, first, that the term "megaloblast" had led to so much misunderstanding that they did not want to use it, and secondly that in all other series the suffix "—blast" was reserved for the earliest distinguishable member, and so the red-cell series did not reflect the progress from "—blast" to "—cyte" that was standardised for the leucocytic series. The committee therefore proposed the terms "rubriblast, prorubricyte, and metarubricyte" for what in the nomenclature used by WHITBY and BRITTON[5] and ISRAËLS are "pro-erythroblast, early, intermediate, and late, normoblasts" respectively. The name "erythrocyte" was retained for the mature red clood-cell. For the megaloblast groups the committee proposed to write the term "pernicious-anæmia type" before rubriblast and the rest.

The committee's proposals were discussed at the January meeting of the Association of Clinical Pathologists in London[6], when Dr. ISRAËLS introduced the subject. He accepted the leucocyte proposals in the main, but disagreed completely with the proposed new names for the red-cell series. He argued that confusion about megaloblasts is now limited to certain less senior American schools and hospitals, that the term "rubriblast" is an unpleasant Latin-Greek hybrid, and that use of the prefix "pernicious-anæmia

1. Israëls, M. C. G. Atlas of Bone-marrow Pathology. London, 1948.
2. *Amer. J. clin. Path.* 1948, **18**, 443.
3. *Ibid.* 1949, **19**, January number.
4. *Blood*, 1949, **4**, 89.
5. Whitby, L. E. H., Britton, C. J. C. Disorders of the Blood. London, 1946.
6. *Lancet*, Feb. 26, p. 350.

Digitized by Google

type " is to be deprecated because it tends to prejudge the diagnosis. The subsequent discussion, in which Dr. C. J. C. BRITTON and Dr. A. H. T. ROBB-SMITH took part, showed that the meeting agreed with Dr. ISRAËLS. The proposals have been published in the American journals,[4] but without comment, and it looks as though American opinion about them were divided.

In the face of this opposition, the American committee's proposals are unlikely to gain unanimous acceptance. But the matter will not be left there; a valuable impetus towards greement has been given and discussions will continue. We began by noting how little disagreement really remains on this question of nomenclature. Next year the International Hæmatology Conference will be held in Cambridge; and, surely, with the groundwork so well prepared, there will then be an opportunity for European and American clinicians and pathologists to meet and settle the details of a nomenclature acceptable to all. Not everyone will agree with Dr. ISRAËLS that current usage, however illogical, is a better basis than an unfamiliar set of terms, however uniform. But agreement is probably practicable on such a basis, and we shall be surprised if the agreed standard nomenclature differs much from that in use in so many countries today.

Malignant Hypertension

FEW surgical procedures have achieved so much popularity with so little publicity as lumbodorsal sympathectomy for hypertension. This major development in sympathetic surgery emphasises the need for closer inquiry into both the causes and the effects of high blood-pressure.

With the reluctant sanction of the pathologists, the term " malignant hypertension " has crept rather uncomfortably into our nomenclature, alongside such entities as " thyrotoxicosis " and " idiopathic steatorrhœa." But there are good reasons for uncertainty. Like many other major advances, ALLBUTT's separation of hypertension without renal involvement (hyperpiesia) from renal hypertension led to an over-simplification, so that the exceptions which should have proved the rule and formed the starting-point for the next advance were for many years ignored. When VOLHARD and FAHR took up the thread in 1914 they recognised " malignant nephrosclerosis " as a vascular rather than an inflammatory form of Bright's disease, but their morbid-anatomical bias led them to the view that the endarteritis and arteriolar necrosis found in the kidneys was the cause of the hypertension. By making a more careful study of the disease in its early stages KIMMELSTIEL and WILSON [1] and ELLIS [2] concluded that the clinical syndrome of malignant hypertension with papillœdema preceded the renal lesions, and they put forward the view that renal damage was the result and not the cause of the hypertension. This interpretation did not, however, convince the pathologists, who were unable to accept the " inflammatory " picture of chronic interstitial nephritis as a sequel to hypertension. When WILSON and BYROM [3] provided experimental evidence that induced hypertension in the rat could give rise to renal lesions identical with those of malignant hypertension in man, a clinical-pathological reconciliation appeared inescapable. In this country the evidence has been generally accepted, and much of the obscurity surrounding chronic Bright's disease has been lifted. In America on the other hand, though WILSON and BYROM's experimental results have been confirmed, their views have had only scant acceptance, largely owing to GOLDBLATT's [4] strange insistence that their experimental renal lesions can be explained by pre-existing pyelonephritis. GOLDBLATT was able to produce arterial necroses in his hypertensive dogs only when *both* renal arteries were so severely constricted that uræmia resulted. He maintains therefore that the lesions are due to the combined effects of hypertension and some humoral factor.

BYROM and DODSON [5] have now answered GOLDBLATT's criticism and have provided direct evidence that raised intravascular pressure can by itself produce renal vascular necrosis. By forcible injection of saline into the carotid artery of the rat, these workers intermittently raised the aortic pressure by 80–90 mm. Hg. After several injections they observed irregular residual pallor of the kidney surface, which they attributed to transient vascular spasm. On histological examination of the kidneys, necrotising arteritis was observed in 10 out of 23 rats. Though the lesions were very few (1 or 2 per section), they closely resembled the arterial necroses seen in experimental hypertension: arcuate and interlobular arteries and afferent arterioles were affected but glomerular lesions were not observed. In 10 animals, one renal artery was occluded by a loop of thread during the injection, to protect the kidney against the increased blood-pressure; and no vascular necroses were observed in the kidneys thus protected. Arterial lesions were not found in other organs, but BYROM and DODSON suggest that vascular spasm similar to that observed in the kidneys may occur elsewhere, and that it may account for some of the acute symptoms of malignant hypertension, especially those associated with encephalopathy.

Though these observations do not exclude the possibility that humoral factors or uræmia may in some circumstances contribute to the production of arterial necroses, they afford convincing evidence that these lesions can result from raised intravascular tension alone. In applying the findings to human disease it must be admitted that comparable renal lesions have not followed induction of experimental hypertension in other animals; but the rat approximates very closely to man in the facility with which hypertension can be induced, particularly as a result of unilateral renal damage. Though we still do not know exactly why hypertension leads to renal vascular damage, papillœdema, and encephalopathy in some patients and not in others, the accumulating experimental evidence confirms the clinical concept that fundamentally malignant hypertension differs from benign hypertension only in the height of blood-pressure, and that repeated or persistent elevation of intravascular tension above a " safety " level—which may vary in different individuals—produces irrever-

1. Kimmelstiel, P., Wilson, C. *Amer. J. Path.* 1936, **12**, 45.
2. Ellis, A. W. M. *Lancet*, 1938, **i**, 977.
3. Wilson, C., Byrom, F. B. *Ibid*, 1939, **i**, 136; *Quart. J. Med.* 1941, **34**, 65.
4. Goldblatt, H. The Renal Origin of Hypertension. American Lecture Series. Springfield, Illinois.
5. Byrom, F. B., Dodson, L. F. *J. Path. Bact.* 1948, **60**, 357.

Digitized by Google

sible vascular lesions and thereby leads to a *qualitative* change in the nature of the disease process. Herein the surgeon may find a more satisfactory rationale for sympathectomy and an explanation of some of his results.

Annotations

THE KING

ON March 8 a bulletin was issued by Sir Maurice Cassidy and his colleagues stating that the King's general health continued to be excellent, and that in the left leg the flow of blood had been restored in the main arteries to a satisfactory degree. In the right leg, however, the main artery was still obstructed, and the circulation was being carried on, less efficiently than in the left leg, through collateral vessels. The bulletin concluded:

> "With a view to improving the blood-supply to the right foot, and to safeguard this for the future, we have advised His Majesty that the operation of lumbar sympathectomy should be performed on the right side. The King has accepted this advice and the operation will be performed at an early date."

Last Saturday morning lumbar sympathectomy was carried out at Buckingham Palace by Prof. J. R. Learmonth (assisted by Mr. A. J. Slessor), with Prof. J. Paterson Ross (assisted by Mr. C. J. Longland); the anæsthetist was Dr. John Gillies. Subsequent announcements made it clear that recovery from the operation was proceeding smoothly, and there is every reason to hope that its object will be achieved. Members of the medical profession must all have recognised the grave possibilities of the King's illness as described at its outset, and will therefore have particular reason to be glad that its course has been relatively favourable, allowing the surgeons to choose, and perform at their own time, a therapeutic operation which should improve function.

The names of Mr. Slessor, Mr. Longland, and Dr. Gillies have not appeared in previous bulletins. Mr. Slessor is medical superintendent of, and assistant surgeon to, the Western General Hospital, Edinburgh. Mr. Longland is first assistant in the surgical professorial unit of St. Bartholomew's Hospital, which Professor Paterson Ross directs. Dr. Gillies is director of the department of anæsthetics at the Edinburgh Royal Infirmary.

NEUROLOGICAL DISORDERS IN PERIARTERITIS NODOSA

THE nervous system is fairly often involved in periarteritis nodosa, as recent reports testify.[1] In an investigation of 16 cases of death from this disease, Parker and Kernohan,[2] at the Mayo Clinic, found that in 5 the nervous system was not affected, while in 4 it was affected only in the terminal stages. In the remaining 7, however, neurological symptoms were present from the start of the illness; in 2 the clinical picture was that of an acute infective process in the brain, which was diagnosed as multiple cerebral abscesses; in the 3rd case the condition resembled clinically a rapidly growing glioma; the 4th was of an elderly patient with signs of peripheral and cerebral arteriosclerosis who died of thrombosis of the basilar artery; in the other 3 the peripheral nerves were involved. Studying the records of 29 fatal cases, Lovshin and Kernohan [3] found that in 15 there had been clinical evidence of peripheral neuritis. In 8 this had taken the more characteristic form, termed by these authors "mononeuritis multiplex," in which various individual peripheral nerves are affected either at the same time or at intervals; in the other 7 there was symmetrical polyneuritis without special distinguishing features. In 4 of these 15 patients clear-cut regression of symptoms and signs had taken place, while in the other 11 the peripheral neuritis gradually or suddenly progressed, or remained stationary till death.

Peripheral-nerve involvement is so common in periarteritis nodosa that this diagnosis has to be considered in any obscure case of symmetrical polyneuritis, especially with fever or disorder of other systems such as the renal and alimentary; where individual peripheral nerves are suddenly affected at varying intervals, and especially when there is fever and pain in the muscles, the diagnosis is highly probable. In explanation of peripheral-nerve involvement in this disease two hypotheses have been advanced. The first is that the unknown toxin or pathological agent which affects the arteries acts independently on the nerves; while the second is that anoxæmia arises in the nerve from closure or narrowing of the nutrient arteries. Lovshin and Kernohan have established beyond doubt the existence of this second mechanism. In 15 of 25 cases submitted to necropsy there had been clinical signs of peripheral neuritis; and in each of these the nutrient arteries showed lesions similar to the arterial lesions elsewhere in the body. The changes were most prominent in the small arteries in the interfascicular connective-tissue; and acute, subacute, and chronic arterial lesions were sometimes found at different levels in the same body. The nerve-fibres showed wallerian degeneration, but the most significant finding, which was not uncommon, was the presence of sharply localised infarcts coinciding with the level of maximal vascular damage.

These studies explain clearly the clinical picture of mononeuritis multiplex in periarteritis nodosa; but they do not clarify the origin of the symmetrical polyneuritis which is almost as common in this disease.

WHERE SHOULD MEDICINE BE TAUGHT?

THERE was a time when medical schools were not affiliated to hospitals; and the change which brought students to the bedside meant a great advance in medical teaching. Dr. C. Fraser Brockington, writing in a Canadian journal,[1] suggests that now another great change is due. In the hospital, life "still revolves around the necropsy and the microscope"; but the emphasis in medicine as a whole is shifting from the pathology of the individual case to "another pathology," as Simon said in his *English Sanitary Institutions*, "than that which our clinics and dead-houses teach us, yet a pathology almost parallel in its teachings"—the social pathology of disease. The hospital sees end-results, and often only selected end-results; for, as Ryle has pointed out,[2] patients in teaching hospitals are admitted because they are "good teaching material"—that is because of the gravity, difficulty, or rarity of their cases. With ætiology and prevention most physicians and surgeons have little serious concern.

The results of failure to prevent disease change with the centuries: thanks largely to environmental advances the student of today sees other diseases than his forerunner of a hundred years ago, when cholera and tuberculosis were rife, and death from septicæmia was a common outcome of surgery. He cannot grasp how many diseases are essentially "social," for, as Ryle notes, many that were once endemic in England—such as cholera, plague, malaria, leprosy, and hookworm—are now aliens, classed as "tropical" or "subtropical" diseases. Their dis-

1. Leishman, A. W. D. *Lancet*, 1937, i, 803. MacKeith, R. *Brit. med. J.* 1944, i, 139. Miller, H. G., Nelson, M. G. *Lancet*, 1945, ii, 200. Turner, J. W. A., Paterson, J. H. *Ibid*, 1946, ii, 143. Tonkin, R. D., Pulvertaft, R. J. V. *Ibid*, 1948, ii, 291.
2. Parker, H. L., Kernohan, J. W. *Proc. Mayo. Clin.* 1949, **24**, 43.
3. Lovshin, L. L., Kernohan, J. W. *Ibid*, p. 48.

1. *Canad. J. publ. Hlth*, 1949, **40**, 22.
2. Ryle, J. A. Changing Disciplines. London, 1948.

Digitized by Google

appearance is an interim victory in the long war fought by the public-health services and the forces of social progress—a war with an interminable campaign still ahead of it. It is therefore unfortunate, Dr. Brockington thinks, that the teaching of medicine is still traditionally centred in the hospital; and he believes that someday (though not yet) it must shift to the health centre.

Meanwhile the student must somehow be taught the preventive outlook while "surrounded by sick people and with the elaborate paraphernalia of curative medicine." The General Medical Council in 1936, the Royal College of Physicians in 1943, the Goodenough Committee in 1944, and the British Medical Association in 1944 all advocated this reorientation of the student's teaching; and gradually, as things happen here, the wheel is turning, the revolution is being achieved. The time has come, Dr. Brockington believes, for universities to adopt local health units and use them for the field training of students in medicine, and for research; and he draws attention to a hopeful proposal, in his own area, to affiliate one division in the West Riding health scheme to Leeds University. Like all exponents of a specialty, he is anxious to see thorough training of the young men who enter it, and thinks that this might be achieved by establishing a diploma in social medicine, open only to graduates of registrar standing, and leading to full specialist status. Without necessarily accepting this suggestion, one may agree with his general thesis.

ANTI-HISTAMINE DRUGS IN THE COMMON COLD

AMONG the many and varied theories concerning the pathology of the common cold, allergy has thus far not won much support. This may well be because of the customary separation of vasomotor or allergic rhinitis from acute infectious coryza of virus origin. Yet some of the symptoms of a virus infection of the respiratory tract may be allergic in origin, as Burnet [1] has suggested from his observations on the symptoms following exposure to living attenuated influenza virus. Lately Brewster [2] in America has carried out a clinical trial of the anti-histamine drugs in the common cold, and he uses his results as an argument in favour of the allergic basis of the nasal symptoms.

Brewster's trial of the anti-histamine drugs followed an earlier report [3] of successful results with one of these compounds. Men, women, and children attached to the U.S. Naval Hospital at Great Lakes, Illinois, were urged to report their colds early to one of three clinics established for the purpose. There they were given one of a series of remedies which were used in succession without selection. The anti-histamine drugs chosen were 'Pyribenzamine,' 'Thenylene,' 'Neoantergan,' 'Histadyl,' and 'Benadryl'; and a combination of codeine sulphate and papaverine hydrochloride was given to every sixth patient to provide a control series treated with a standard medicament. At least three doses of 50 mg. of the anti-histamine drug at 4-hour intervals were given by mouth, and a cold was considered to have been aborted or "cured" if all signs and symptoms disappeared within 24 hours of the beginning of treatment and remained absent for at least 48 hours after treatment had ended. Success in aborting the cold with the anti-histamine drugs depended on the stage at which therapy was begun. Thus cures were obtained in 19 of 21 people treated within an hour of the onset of symptoms, 48 of 55 treated within two hours, 116 of 156 treated within six hours, and 165 of 234 treated within twelve hours. The control capsules gave "cures" in 1 out of 2 people treated within an hour of the onset, 5 of 12 within six hours, and 7 of 22 within twelve hours. In none of the controls treated more than twenty-four hours after the onset was benefit obtained, though a few of those receiving anti-histamine drugs at this time were "cured."

The difficulty of establishing a diagnosis within the first few hours of the cold was met by accepting the patient's diagnosis provided that examination revealed no evidence to disprove it. There are many other points about this trial which could be criticised, such as the inequality of the numbers of treated and control subjects and the uniform success of all the anti-histamine drugs, though their therapeutic powers in most other conditions in which they have been used vary widely. Those whose early hours of suffering from the cold are as characteristic as those of the broadcaster whose head began to steam whenever he ate marmalade will no doubt welcome this report. Others who see red whenever the word allergy is mentioned will derive little comfort from it. A word of caution concerning the side-effects of these compounds is needed lest those who try this latest nostrum find the cure worse than the disease. One of the American subjects became disorientated and confused after taking 200 mg. of an anti-histamine drug in four hours. Others complained of drowsiness for which amphetamine was prescribed; we have previously pointed out that this drowsiness might be dangerous in car drivers and others.

SYSTOLIC MURMURS

"A LOUD systolic murmur at the apex should be considered organic in nature until it can be proved of other origin. The patient should be treated accordingly even when evidence of past rheumatic fever, enlargement of the heart, diastolic murmur, abnormal electrocardiogram, or heart failure is lacking." This advice, which tallies with the experience of life-assurance societies, is given by Master [1] in the light of his war-time service with the U.S. Navy. It is not always easy to decide what constitutes a "loud" systolic murmur, but American workers appear to have found Freeman and Levine's [2] classification satisfactory. This divides systolic murmurs into 6 grades of intensity; and according to Levine [3] himself different observers rarely differ in their terminology by more than one grade. Intensive use of this scale in the late war showed that murmurs falling into grades 3–6 are likely to be associated with organic disease of the heart. Master points out that systolic murmurs of organic origin may be heard only after exercise; so also may a systolic murmur in a healthy person, but here the murmur is never loud and is always transitory. Cardioscopy may also help, although in early mitral disease no abnormality of outline may be detected on screening or in the X-ray film. Two early signs of mitral disease that should always be sought are: (1) diminution of the space beneath the left main bronchus, as seen in the left oblique position, and (2) straightening of the left border of the heart in the anteroposterior position. As to differential diagnosis, most of the other conditions likely to account for a systolic murmur—such as hypertension, thyrotoxicosis, and anæmia—can usually be excluded by careful history-taking and examination. Where there is any question of the supposed murmur being actually a split, doubt may be resolved by a phonocardiogram. A funnel-shaped chest, kyphoscoliosis, or other deformity can also mislead the unwary.

Experts still differ on the mechanism by which murmurs are transmitted. Both Master and Levine emphasise that transmission is mainly a reflection of intensity, and Levine adds that bony structures are the best peripheral conductors. Kerr and Harp,[4] however,

1. Burnet, F. M. *Med. J. Aust.* 1943, 1, 385.
2. Brewster, J. M. *Nav. med. Bull., Wash.* 1949, 49, 1.
3. Brewster, J. M. *Ibid*, 1947, 47, 810.

1. Master, A. M. *Arch. intern. Med.* 1948, 81, 518.
2. Freeman, A. R., Levine, S. A. *Ann. intern. Med.* 1933, 6, 1371.
3. Levine, S. A. *Brit. Heart J.* 1948, 10, 213.
4. Kerr, W. J., Harp, V. C. jun. *Amer. Heart J.* 1949, 37, 100.

Digitized by Google

are of the opinion that "the sounds which are transmitted through bone are of negligible importance as compared with those propagated through the arteries"; and they conclude that the most important tissues in propagation are the myocardium, the blood-vessels, and the blood itself, and that the rate of propagation is that of the pulse-wave. In children, where soft systolic murmurs are commoner than in adults, the problem is more complicated. In 320 children with "functional" systolic murmurs, Messeloff [5] found that the murmur was always in grades 1–3, and was of short duration in 92% of cases; but, he adds, organic murmurs in children may occasionally be faint and short.

Mackenzie and his school in this country may have gone too far in minimising the significance of systolic murmurs; but they were wholly justified in arguing that to subject a healthy child to a life of unnecessary cardiac invalidism is as blameworthy as to overlook organic disease and allow a child with rheumatic heart disease to lead an overactive life; Mackenzie and his successors have liberated a host of healthy youngsters from the tyranny of the stethoscope. Master rightly holds that the same principle applies to young adults. The discovery of a loud systolic murmur betokening organic disease is only the first step; the next is to determine the functional capacity of the heart, and it is on this basis that the patient should be advised; organic heart disease sometimes proves quite compatible with the attainment of a ripe old age—and that without any serious restriction.

HOW TO TELL THE WORLD

"IN selling 'Health,' you start knowing your product is good," Mr. R. W. King remarked at last Monday's symposium on "Informing the Public," arranged—and attended—by the Middlesex Public Health Department. A good slogan, or some other good idea, he said, will always help to sell something worth having; but no idea, however good, will sell a bad product. This reassuring thought was slightly offset by Dr. Charles Hill's earlier reflection that we know very little about the maintenance of good health; and that in any case people much prefer to hear about ill health. He thinks we might make a sound start in health propaganda by teaching human biology in schools to children between the ages of 11 and 16—not with a particular bias towards sex instruction, but as a straightforward school subject. Exhibitions on health subjects, he believes, attract only the converted (apart from the searcher after samples, who will go anywhere). On the whole he was inclined to think that the private talk, preferably given by the doctor, is the most effective form of health teaching, though he had a not unnatural tenderness for the broadcast. Advice on broadcasting from so brilliant an exponent deserves attention: Dr. Hill believes that a speaker on health should talk simply, and be content to use the unambitious jest as it offers, to speak the English he commonly speaks, and to make relatively few points, preferably in a short time. He himself likes to speak for only five minutes. It is certainly essential to be simple, for as Dr. W. Hartston, who arranged the symposium, explained, those to be addressed are mainly simple people. Of a population of half a million recruits whom he examined during the war, and classified in five grades according to intelligence, about a third were in the two lowest grades. Grade 1, he said, needs no health propaganda; grade 2 may; but the bulk of those addressed are in grades 3, 4, and 5. Propaganda must be arranged according to the needs and capacity of these grades. In the past public-health propaganda has not on the whole been good or particularly successful. He reminded the meeting that diphtheria immunisation was first introduced in 1913; and in 1937 we were still getting an annual death-rate of 3000 from diphtheria. Yet expensive, determined campaigns will get results: in 1946 there were only 455 deaths from diphtheria: in Harrow during 1946–48 there were no deaths at all, and in 1948 no *cases* of diphtheria. The plea for simple, human, popular teaching was endorsed by Mr. Macdonald Hastings, editor of the *Strand Magazine*.

The advice of Mr. A. A. MacLoughlin, public relations officer to the Middlesex County Council, on the manners of the official to the citizen, might change the whole mood of the country if it could be widely adopted. As he said, the person who is casually or indifferently received at the county offices will go away with a bias against health teaching which nothing can counteract.

Perhaps the saddest note at the conference came from a dental officer who begged that no propaganda should be initiated on behalf of his profession: it is useless to offer a service when there are not enough dentists to carry it out. He suggested, however, that the public need educating in the prevention of dental caries; and here is the kind of subject that must commend itself to propagandists. "Keep Your Teeth for Life" might be the slogan—if we knew a little more about how to do it.

POSTGRADUATE EDUCATION IN AUSTRALIA

THE great distances which separate the Australian States hinder informal contacts, and an official body with a reliable administrative framework is a valuable link between the scattered medical communities. The committees for postgraduate education in the different States have therefore joined to form the Australian Postgraduate Federation of Medicine. Provision has also been made for similar bodies in New Zealand and elsewhere to become members. The object of the federation is to encourage and advance postgraduate medical education, work, and research, and it looks forward especially to being able to help in arranging visits by lecturers from overseas to all the centres of the continent. Another side of its work will be to offer advice and recommendations to Australian postgraduates when they visit London or other centres abroad. Each year the federation will nominate a State whose postgraduate committee will then elect the federal executive committee. The postgraduate committee in medicine in the University of Sydney are the first to be nominated; Colonel A. M. McIntosh has been elected the first president, and the hon. secretary is Dr. V. M. Coppleson, 131, Macquarie Street, Sydney.

The barony conferred on Sir John Boyd Orr, M.D., F.R.S., in the New Year's Honours has been granted by the name, style, and title of Baron BOYD-ORR, of Brechin Mearn, in the county of Angus.

Dr. James Craigie, F.R.S., has been appointed general superintendent of investigations and director of the central laboratory of the Imperial Cancer Research Fund. He will take up his appointment in August when Prof. W. E. Gye, F.R.S., retires.

Sir Henry Dale, F.R.S., has been elected a life governor of the fund.

The death is announced from Melbourne of Sir Sidney Sewell, a past-president of the Royal Australasian College of Physicians.

THE INDEX and title-page to Vol. II, 1948, which was completed with THE LANCET of Dec. 25, is published with our present issue. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

5. Messeloff, C. R. *Amer. J. med. Sci.* 1949, **217**, 71.

Digitized by Google

Special Articles

HOSPITAL MEDICAL AND DENTAL STAFF
TERMS AND CONDITIONS OF SERVICE

HAVING considered the recommendations of the Spens Committee on the Remuneration of Consultants and Specialists, the Ministry of Health has issued the terms and conditions of service it proposes for hospital medical and dental staffs in the National Health Service. These terms and conditions would operate retrospectively from July 5, 1948.

Discussions with the Joint Committee for Consultants and Specialists, which includes representatives of the Royal Colleges, the Scottish Royal Corporations, and the British Medical Association, are still proceeding, and the proposals do not represent final agreement with the profession's representatives. They are being published at this stage for the information of the profession as a whole.

The essential proposals (omitting certain details) are set out below. In considering them it should be noted that:

1. The terms and conditions of service are subject to minor adjustments for Scotland.
2. All salary scales will apply equally to men and women, and uniformly throughout England, Wales, and Scotland.
3. Under the National Health Service Superannuation Scheme, over and above any salary specified here, the employing authority will be paying a contribution, equal to 8% of the salary, into the superannuation fund. The employee's contribution (6%) will be deducted from remuneration.

SPECIALISTS

Main Scale for Staff Specialists at Hospitals, including Dental Specialists

Specialists appointed at age 32: £1700 × 125–£2075 × 150–£2375 × 125–£2750 per annum non-residential.

Specialists appointed at age 31 or earlier to start at £1550 or £1400 respectively.

Specialists first appointed after age 32: the hospital authority to be able to fix the starting salary at any of the four next incremental points in the scale, (i) by reason of age, special experience, and qualifications, or (ii) by reason of age alone, where seniority has been lost because of service with H.M. Forces; provided that the starting salary shall in no case be higher than the specialist would receive on age alone.

Special Distinction Awards

An Advisory Committee on Awards for Consultants and Specialists has been set up to advise the Minister of Health and the Secretary of State for Scotland which specialists engaged in the National Health Service should receive awards for professional distinction, having regard to the desirability that 4% of all specialists in the service should receive the highest award (£2500 per annum in addition to the "basic salary"), a further 10% the second award (£1500 per annum), and a further 20% the third award (£500 per annum). These awards will be paid as an element of remuneration additional to the main scale and will be superannuable.

TRAINEE SPECIALIST GRADES (INCLUDING DENTAL)

Grade 3 (as defined in the Spens report: posts obtained normally not less than one year after registration and held normally for one year only): £670 per annum non-residential.

Grade 2 (posts obtained normally not less than two years after registration and held normally for two years): £775 per annum non-residential in the first year; £890 in the second and any subsequent years.

Grade 1 (posts obtained normally not less than four years after registration and held normally for three years): £1000 per annum non-residential in the first year; £1100 in the second year; £1200 in the third year; £1300 in any subsequent years.

Trainee specialists not to proceed from one grade to another by automatic promotion. Each grade of post demands a distinct level of ability and experience. A trainee specialist in a lower grade to be considered on merit, along with other applicants, for a vacancy in a higher grade.

A trainee specialist holding an appointment in grade 1 and subsequently appointed to a grade 2 post, to be paid the higher salary appropriate to grade 2 (i.e., £890 per annum) while he holds the post in that grade.

OTHER NON-SPECIALIST GRADES

Junior House-officer (including Dental): £350 per annum non-residential for the first post held; £400 for the second post; £450 for the third and any subsequent post. In each case, a deduction of £100 per annum in respect of residential emoluments. Each post to be tenable for six months.

The Minister will be prepared to authorise, in exceptional circumstances, salaries up to £50 per annum higher, where a post cannot be filled otherwise.

Junior Hospital Medical Officers, who have held house-appointments but who are not trainee specialists, and who have less responsibility than other hospital officers of non-specialist status: £700 (for an officer appointed not less than two years after registration) × 50–£1000 per annum non-residential.

Senior Hospital Medical Officers (senior officers performing clinical duties, who are not of staff specialist status but are not trainees): £1300 per annum (at age 32) × 50–£1750 (non-residential), the position on this scale to be determined by age (subject to arrangements in section headed Determination of Salaries &c.).

Medical Superintendents and Deputy Medical Superintendents.—The objective will be to reduce to a minimum the time to be given by medical staff to administrative duties, and to enable them to devote their energies to clinical work in their appropriate grade. Subject to further consideration in the case of mental hospitals and mental-deficiency institutions, medical superintendents and deputies to be remunerated for clinical work as specialists or senior hospital medical officers, according to their grading; for administrative work, to be remunerated at the appropriate rate for hospital administrative staff; where, however, a whole-time officer is engaged almost wholly in clinical work and gives only a small proportion of time to administrative duties, his appropriate clinical remuneration not to be affected.

TRANSFERRED OFFICERS

Officers who were transferred under section 68 of the National Health Service Act, 1946, and who immediately before July 5, 1948, were receiving salaries better than those now introduced, to be entitled to retain their previous salary on a personal basis, for so long as they remain in the same appointment or another appointment of the same or greater responsibility as the one they held at the appointed day; but otherwise to conform to the new rates of remuneration on taking up a new appointment, or on promotion.

PART-TIME APPOINTMENTS, &C.

Part-time Specialist Appointments

Before offering a part-time specialist appointment the board to assess in terms of hours per week what is the average amount of time required by an average practitioner to perform the duties attaching to the post. In assessing the average amount of time to perform the duties attached to the post, to take into account out-patient clinics, ward rounds, operating sessions, laboratory work, and so on, in their hospitals, including occasional visits to outlying hospitals for consultation,

Digitized by Google

diagnosis, or operative work. Also to include time given—e.g., as consultant adviser to the board on special branches of the service or by way of "pastoral visits" to cottage hospitals; and time necessarily spent in travelling from home or private consulting-room (whichever is the nearer) to the hospital or hospitals served (unless the journey is one which he would undertake irrespective of his work for the board). To *exclude* time spent in emergency calls to patients in the beds in their charge (except where any exceptionally heavy liability to recurring emergency work of this sort is anticipated), or in committee work, or in care of private patients in pay-beds or as outpatients. Also to exclude domiciliary visiting, for which special fees are payable.

The object is to express this aggregate number of hours per week as a number of notional "half-days" per week. It will not be necessary at any time to "clock in" the actual number of hours worked on any particular day or in any particular week by any particular specialist—the number of "half-days" is merely the means of expressing the duties attaching to the post in terms which enable remuneration to be calculated without meticulous adjustments up or down from time to time.

To arrive at the number of notional "half-days" from the aggregate of hours so assessed, the total to be divided by $3^1/_2$, the specialist being given the benefit of the marginal overlaps. In other words, the relation of "half-days" to hours to be as follows:

No. of hours weekly	*No. of notional half-days on which salary will be reckoned*
Up to $3^1/_2$	1
Over $3^1/_2$ and up to 7	2
„ 7 „ „ „ $10^1/_2$	3
„ $10^1/_2$ „ „ „ 14	4
„ 14 „ „ „ $17^1/_2$	5
„ $17^1/_2$ „ „ „ 21	6
„ 21 „ „ „ $24^1/_2$	7
„ $24^1/_2$ „ „ „ 28	8
„ 28	9

The part-time salary to be determined by applying to the number of half-days calculated in this way the formula recommended in the Spens report—i.e., the part-time salary to be the following proportion of the whole-time salary appropriate to the specialist:

$$\frac{\text{number of half-days}}{11} + \frac{\text{one quarter of number of half-days}}{11}$$

or

$$\frac{\text{number of half-days}}{11} + \frac{\text{one quarter of (11—number of half-days)}}{11}$$

whichever is the less, subject to the maximum referred to below.

The following is an example of application of above:

A physician divides his time as follows:

Work	*Estimate of time required by an average practitioner*	*Total weekly time (hours)*
2 outpatient clinics	2 hours weekly { +$^1/_2$ hour's travelling in each case*	$4^1/_2$
	$1^1/_2$ „ „	
"Pastoral visits" to cottage hospitals	One day of seven hours fortnightly, including travelling*	$3^1/_2$
Irregular hospital visits	2 hours weekly, including travelling*	2
Charge of beds	9 hours weekly, + $^1/_2$ hour's travelling daily for 6 days*	12
Adviser to board	8 hours monthly	2
	Total	24 = 7 "half-days"

* Travelling time would of course depend on the particular circumstances of the individual concerned.

For this the physician would receive eight-elevenths of the appropriate whole-time remuneration—i.e., $\frac{7}{11} + \frac{(11-7)}{44} = \frac{8}{11}$.

Part-time Appointments as Senior Hospital Medical Officer

The above formula for arriving at part-time salaries to be applied to all part-time appointments as senior hospital medical officer.

Exceptional Consultations

Specialists who have no contract with the board, but who are called in exceptionally to hospitals or clinics for a special visit (e.g., because of their unusual experience or interest) to be paid at the rate of 5 guineas per visit (including any operative work).

As a normal practice, *retired consultants* to be offered honorary (unpaid) appointments in respect of exceptional calls on their services of this kind, which would give them in return the right to use private pay-beds from time to time.

A *general practitioner* not on the staff of a hospital but called in exceptionally to render a specific service in emergency to be paid at the rate of £2 per visit, unless he is debarred from accepting remuneration by his terms of service under part IV of the Act.

Locum-tenens Arrangements

Normally, leave periods to be covered by the normal contract of service providing for practitioners to deputise for each other. Payment at the rate of 5 guineas per half-day, however, to be made to a locum engaged by a board during a specialist's temporary absence when it is impossible to arrange for his work to be adequately performed by other members of the board's staff within the terms of their contract of service.

A locum engaged by a hospital authority during the temporary absence in similar circumstances of a general practitioner holding an appointment on the staff of a hospital to be paid at the rate of $3^1/_2$ guineas per half-day.

Maximum Remuneration for Part-time Appointments

The maximum to be $9^1/_2$ elevenths of the whole-time salary appropriate to the grade. This maximum *not* to include payments made to a specialist in respect of exceptional consultations performed for a board with whom he is not in contract, payments made in respect of work as locum tenens, and payments for domiciliary visits. Where a specialist holds part-time appointments with more than one board, which together are not equivalent to a whole-time appointment, this maximum to apply to the aggregate remuneration from all the boards concerned.

In special circumstances a board, with the Minister's consent in each case, to have discretion to offer a higher rate of part-time remuneration than that normally applicable.

DOMICILIARY VISITS

Payment to be made separately for domiciliary visits by part-time specialists, but no additional payment for whole-time specialists (the basis being that the whole-time duties will be adjusted to include domiciliary visiting where required). Payment to be on the following basis:

Fee for consultation, 4 guineas, with an additional fee of (*a*) 2 guineas where any operative procedure other than obstetric is undertaken or where the specialist uses his own electrocardiograph or portable X-ray apparatus; (*b*) 4 guineas for an obstetric operation. The additional fee of 2 guineas or 4 guineas to be payable once only in respect of each patient for the current illness.

Boards to make payments, additional to the fee for the visit and to the normal travelling and subsistence expenses, of 1 guinea for a journey of 20–40 miles' radius, 2 guineas for a journey of 40–60 miles' radius, and so on, with an additional guinea for every 20 miles.

Maximum remuneration under this head (excluding travelling and subsistence allowances and additional mileage payment) to be 200 guineas in any quarter or 800 guineas in any year, whichever the specialist prefers.

CLINICAL SPECIALISTS ENGAGED IN TEACHING

Whole-time Clinical Posts in Medical or Dental Schools

As already announced by the Chancellor of the Exchequer, the rates of salary to which the University

Digitized by Google

Grants Committee will have regard in making grants to universities are as follows (operating from April, 1, 1949):

Professors.—Within the range of £2250–2750.

Lecturers.—£600 to a maximum within the range of £1500–2000 (or £2500 for posts carrying special responsibility).

Readers.—Within the range of £1500–2000 (or £2500 for posts carrying special responsibility).

In addition holders of these posts to hold an honorary (unpaid) appointment with the appropriate hospital board or boards, but to receive from the board payment of appropriate expenses, like other specialists, for hospital work. Also to be eligible for distinction awards, the additional remuneration being paid by the university or school and reimbursed to them by the board.

Where exceptionally teachers (including part-time clinical professors or heads of university clinical departments) devote a large portion of their time to university work, to be paid the relevant proportion of the whole-time salary and distinction award by the same method as their whole-time colleagues.

Part-time Clinical Teaching Posts

Specialists performing teaching duties concomitantly with, or separately from, their clinical work to be remunerated by hospital boards like other specialists (including distinction awards and expenses) but in addition to be remunerated by the university or school in recognition of their teaching duties at a rate which appears to the university or school to be appropriate to those duties.

GENERAL PRACTITIONERS ON THE STAFFS OF HOSPITALS IN THAT CAPACITY (PART-TIME)

General-practitioner Hospitals (Cottage Hospitals).—Remuneration in respect of services rendered other than those paid for by the executive council: the hospital management committee to create a staff fund by making a payment of £25 per annum for each bed (other than private pay-beds) occupied on the average in the hospital, the fund to be shared among the general-practitioner staff as they may themselves determine. It is expected that general-practitioner hospitals should have an open staff.

Part-time Medical Officers of Convalescent Homes or other Types of Hospital where no other Rate is Appropriate.—£175 per annum per weekly "half-day" up to a maximum of £1575 per annum.

GENERAL DENTAL PRACTITIONERS EMPLOYED AT HOSPITALS

£150 per annum per weekly "half-day" up to a maximum of £1350 per annum.

Where there is no general dental practitioner on the staff of a general-practitioner hospital the general dental practitioners of the district to be allowed at the discretion of the hospital management committee to have their patients admitted to the hospital where inpatient treatment is necessary.

DETERMINATION OF SALARIES PAYABLE FROM JULY 5, 1948

Specialists.—The boards, in carrying out their review of existing staff, to ascertain the age of each specialist and the date on which he first accepted a staff appointment with full clinical responsibility. Assuming there has been no break in service, the salary payable from July 5, 1948, to be the salary which the officer would have been receiving on that date had the above system of remuneration been in operation since the date of his first appointment. In the case of specialists who were first appointed after age 32, the boards, in determining what their starting salaries would have been, to exercise their discretion as they would have exercised it had they been the appointing authority.

Senior Hospital Medical Officers.—Boards or hospital management committees to have discretion to decide at which point in the salary scale for senior hospital medical officers existing staff should start, provided that the starting salary shall in no case be higher than that which the officer would receive were his position on the scale determined by age alone.

Junior Hospital Medical Officers.—Existing staff in this grade who immediately before July 5, 1948, were receiving less than the minimum remuneration for the grade to start at the minimum of the salary scale; and those who were receiving more than the minimum to enter the scale at the salary they were receiving immediately before July 5, 1948, rounded off, at the discretion of the board or management committee, to the next incremental point in the new scale.

INCREMENTAL DATES

In the case of officers holding appointments at July 4, 1948, the incremental date to be July 5; in the case of new appointments or promotions, the date on which the new post was entered into.

PRIVATE PRACTICE AND RETENTION OF FEES

Whole-time officers not to be entitled to enter into arrangements with private patients under section 5 (2) of the Act to undertake private practice. The contract of a whole-time officer normally to provide that he may be called on to treat patients occupying section 5 beds without additional remuneration. A part-time officer to be able to agree with a board that he will treat patients in section 5 accommodation, in return for remuneration by the board, without charging the patients a private fee for his professional services.

Payments for Professional Services not within the Scope of the Hospital and Specialist Service

It has been necessary to consider the question of payments from outside sources to hospitals, and/or to members of hospital and medical staffs, for the rendering of medical reports on patients who are receiving treatment, and for the examination, diagnosis, and rendering of reports on persons referred to hospitals for these purposes only.

All work of this kind to be divided into the following two categories:

I. Work which may properly be regarded as within the scope of the hospital and specialist services provided under section 3 of the Act.

II. Work which cannot be regarded as within the scope of the service but which may for convenience be done at hospitals or by members of hospital medical staff.

The principles on which these two categories may be distinguished are indicated, and illustrated by examples, in a schedule. Category I includes examination and reports on persons referred *from a medical source* for a second expert medical opinion; on persons resorting to or referred to a mass radiography unit; and on offenders referred by court under sections 24 and 26 of the Criminal Justice Act, 1948.

Services in category I to be available free of charge to any person reasonably requiring them. Members of hospital medical staffs to be permitted to provide services in category II, at hospitals or elsewhere, where their provision would not interfere with other hospital activities or with the proper discharge of hospital duties; but services in this category to be available to persons requiring them (including Government departments) only on payment of appropriate charges.

Where hospital laboratory or radiological facilities are used, such charges represent two elements: (*a*) payment for professional services, and (*b*) payment of hospital costs. Where hospital laboratory or radiological facilities are not required, no charge to be made for the use of hospital premises, payment being in respect of professional services only.

Digitized by Google

Whether the practitioner concerned be a whole-time or a part-time officer, all charges in respect of professional services to be retained by him or remitted to him by the board or committee according as the money is received by the practitioner himself or (as is expected to be the more convenient course when the work is done in hospital) by the board or committee.

Where hospital laboratory or radiological facilities are used, one-third of the payment made to be retained by or remitted to the board or committee, in respect of hospital costs.

Other work in category II includes lectures given by members of hospital staffs to nurses, &c., or to the lay public; and services performed by them for Government departments as members of medical boards.

RETIRING AGE

When an officer reaches age 65 his regular contract to come to an end, provided that (*a*) the board may, with his consent, extend his contract of service (or offer a modified contract) for one year or any less period, and so from time to time until age 70, or (*b*) the board may allow him an honorary contract as mentioned above. These ages to be reduced in respect of practitioners who are "mental health officers" under the superannuation regulations.

TENURE OF POST

No fixed period of tenure to be specified in the contract of service of a specialist. Where a specialist felt that his appointment was being unfairly terminated by a board, he would be entitled to send a full statement of the facts to the Minister, who would obtain the written views of the board and place the case before a professional committee (consisting of representatives of the Ministry and representatives of the profession, under the chairmanship of the Chief Medical Officer) for their advice. The committee to have discretion to interview both parties if they thought fit. In the light of their advice the Minister to confirm the termination of services, or direct reinstatement, or arrange some third solution agreeable to the parties concerned, such as re-employment in a different post. This procedure to be completed before the board's decision to terminate the specialist's services was carried into effect.

RESIDENTIAL EMOLUMENTS

The above rates are non-residential. Where an officer is provided with residential or other emoluments by the hospital (i.e., the officer's main hospital), a reasonable inclusive charge to be fixed by the hospital management committee (or board of governors) for the accommodation or other emoluments (including meals), except that the charge for house-officers to be a fixed rate of £100 per annum.

LEAVE

Annual Holiday Leave

Officers in receipt of salaries of less than £1000: at the rate of 4 weeks per annum (in addition to statutory and general national holidays or days in lieu). Officers in receipt of salaries of £1000 or more: at the rate of 6 weeks per annum (in addition to statutory and other general national holidays or days in lieu). In the case of officers performing part-time services, leave entitlement to be based not on the actual salary but on the corresponding whole-time salary rate.

Absence for such purposes as attendance at court, &c., not to be taken into account for the purposes of annual leave.

The annual leave year to run from April 1 to March 31. New entrants to the service to be entitled to annual leave proportionate to the completed months of service during the year of entry, and thereafter on the normal scale.

Compassionate Leave, and any Special Leave other than "Study Leave"

Leave without pay (normally not counting either for increment or pension) to be granted at the discretion of the board. Leave with pay to be granted by the board with the approval of the Minister.

Sick Leave

An officer absent from duty owing to illness, injury, or other disability, to be entitled to an allowance as follows:

During first year of service: 1 month's full pay and (after completing 4 months' service) 2 months' half pay.

During second year: 2 months' full pay and 2 months' half pay.

During third year: 3 months' full pay and 3 months' half pay.

During fourth to sixth years: 4 months' full pay and 4 months' half pay.

During seventh to tenth years: 5 months' full pay and 5 months' half pay.

After ten years: 6 months' full pay and 6 months' half pay.

The board to have discretion to extend the application of the foregoing scale in an exceptional case.

Instructions are given for calculating the allowance, which, when added to any sickness benefit, injury benefit, compensation payments, or similar payments, including allowances for dependants, is not to exceed the officer's normal monthly salary.

Conditions on which sick-leave allowance is to be paid include the following:

An officer who is prevented by his illness from reporting for duty to notify immediately the officer prescribed for this purpose by the employing authority. If his absence continues after the third day, to submit forthwith a medical certificate as to the nature and probable duration of the illness. Thereafter medical certificates to be submitted at intervals of seven days or at such longer intervals as in any case may be decided by the employing authority. On his returning to duty, the officer to submit a medical certificate of fitness if required.

An officer entering a hospital or similar institution to submit a medical certificate on entry and on discharge in substitution for periodical certificates.

A case of a serious character, in which a period of sick leave on full pay in excess of the normal period of benefit would, by relieving anxiety, materially assist a recovery of health, to receive special consideration by the employing authority.

An allowance not to be paid in a case of accident due to active participation in sport as a profession nor in a case in which contributory negligence is proved, unless the employing authority by resolution decide otherwise.

A period of absence due to injury sustained by an officer in the actual discharge of his duty and without his own default not to be recorded for the purposes of this scheme.

The employing authority to be able at any time to require an officer who is unable to perform his duties as a consequence of illness to submit to an examination by a medical practitioner nominated by the authority.

If it is reported to the employing authority that an officer has failed to observe the conditions of this scheme or has been guilty of conduct prejudicial to his recovery and the authority is satisfied that there is substance in the report, the payment of the allowance to be suspended until the authority has made a decision thereon, provided that before making a decision the employing authority shall advise the officer of the terms of the report and shall afford him an opportunity of submitting his observations thereon and of appearing, or being represented, before the authority or its appropriate committee. If the employing authority decide that the officer has failed without reasonable excuse to observe the conditions of the scheme or has been guilty of conduct prejudicial to his recovery, then the officer to forfeit his right to any further payment of allowance in respect of that period of absence.

This scheme not to apply to an officer who is required to absent himself from duty following contact with a case of notifiable disease. In such a case the period of absence to be regarded as special leave with full pay.

EXPENSES

Travelling, subsistence, and other expenses to be paid to meet actual disbursements of officers engaged in the

Digitized by Google

service of the board and not to be regarded as a source of emolument or reckoned as such for purposes of pension. In preparing claims, officers to indicate adequately the nature of the expenses involved; claims to be submitted normally at intervals of not more than one month, and as soon as possible after the end of the period to which the claim relates.

Travelling Expenses

Travelling expenses to be paid by the board for any journey in the board's service, provided that

In the case of a *whole-time officer*, expenses incurred in travelling between his place of residence and the hospital where his principal duties lie not to be allowed except as indicated below.

In the case of a *part-time officer*, travelling between his private consulting-room or place of residence and any hospital where he is employed, whichever is the less, to be regarded as a journey in the board's service, provided that no expenses should be allowed for any such journey or part of such journey which would have been undertaken by the officer irrespective of his employment with the board.

Expenses incurred in travelling from holiday leave to duty or vice versa not to be allowed unless the officer was recalled for special reasons.

Taxi or cab fares to be payable only in cases of urgency or in other cases in which transport is reasonably required and an adequate public service is not available, but where these conditions are not fulfilled an officer using a taxi or cab to be entitled to claim the sum he would have been paid had he travelled by public-service vehicle.

An officer making an overnight journey by rail and engaging sleeping-car accommodation to receive the cost, but any subsistence allowance payable to him for that night to be reduced by one-third.

Except where a private car is used, the sum paid not to exceed the amount disbursed—e.g., if the practitioner is entitled to travel first-class but in fact takes a third-class ticket he can only claim third-class fare. First-class fares to whole-time officers with salaries of £760 and over, and part-time officers of corresponding status.

Car Allowances

Officers, whether whole-time or part-time, to be classified as "regular users" or "casual users" according to whether their annual official regular mileage is estimated to exceed 2000 miles or not.

All regular users of motor-cars, of whatever horse-power, to be paid an annual allowance of £52 and 3½*d.* per mile. The annual allowance to be paid by quarterly instalments in advance. The mileage allowance to be paid monthly or quarterly. The annual allowance to continue during absences on annual leave or sick leave or while the car is out of use being repaired or overhauled, except that where any one period of non-user exceeds two months the sum of £4 6*s.* 8*d.* to be deducted for each complete month after the first (e.g., if a car is out of use for 3½ months, £8 13*s.* 4*d.* should be deducted from the allowance).

If at the end of the year it is found that an officer who has been treated as a regular user has not completed 2000 miles, he should not be called upon to repay any part of the annual allowance. This does not preclude review and reclassification of any officer at any time where appropriate.

Casual users to receive no annual allowance, but to be paid 7½*d.* a mile for the first 3120 miles a year and 3½*d.* a mile thereafter.

Where a "regular user" has contracts with more than one board which require him to make a claim to more than one board, the board with whom he has his main contract to be responsible for paying the annual allowance of £52 and for verifying from time to time from the other boards concerned that the officer is still a regular user, all the boards concerned to pay 3½*d.* a mile for actual mileage in the claims appropriate to them.

If an officer uses a private motor vehicle in circumstances where travel by a public service would be appropriate, a mileage allowance of 1½*d.* a mile to be payable irrespective of the type of vehicle.

Where other officers, or members of an employing authority are conveyed in the same vehicle on the business of the National Health Service, and where fares by a public service would otherwise be payable, an allowance of ½*d.* a mile for each passenger to be payable.

The "allowance year" for the purpose of car allowance to be regarded as the year to March 31. In the first year in which an officer is authorised to use his car, a proportionate reduction of the 3120 miles or adjustment of the annual allowance (as the case may be) to be made.

"Public service" refers to railways, steamships, omnibuses, and tramways.

Payment of Mileage Allowances to Whole-time Officers for Journeys from Home to the Hospital where Principal Duties Lie

Where a whole-time officer travels from his home to the main hospital, either before and/or after an official journey, travels direct from his home to the place visited, or returns direct from that place to his home, mileage allowance to be payable for the whole distance travelled, subject to a maximum based on the return journey from the officer's main hospital to the place visited plus 20 miles.

Ordinary mileage allowance to be paid for the distance equal to the return journey between the officer's main hospital and the place visited. The additional 20 miles to be paid for as follows: (i) if the officer is the holder of a current season ticket for travelling between his home and hospital—at the appropriate rate as detailed above; (ii) if the officer is not a season-ticket holder—the appropriate rates less 1½*d.* a mile.

Subsistence Allowances

For officers in receipt of a salary of £760 per annum or over:

An allowance not exceeding 30*s.* to be payable in respect of each night when the officer is necessarily absent from his home or main hospital on the business of the employing authority. The allowance to be reduced to 25*s.* 6*d.* a night after the first 7 nights at one place and to be further reduced after 28 nights if the stay extends beyond that period.

A night allowance to be deemed to cover a single period of absence of 24 hours.

A day allowance in respect of duties not involving a night's absence to be payable at the rate of 3*s.* 6*d.* when an officer is necessarily absent from his home or main hospital for more than 5 hours but not more than 8 hours, and at the rate of 8*s.* 4*d.* when his absence exceeds 8 hours.

For officers in receipt of a salary of less than £760 per annum, the following rates to be substituted:

A night allowance of 24*s.* (18*s.* after the first seven nights and up to a maximum of 28 nights in one place).

A day allowance of 2*s.* 6*d.* for an absence of more than 5 hours and less than 8 hours, and of 6*s.* for an absence exceeding 8 hours.

Payment of the above allowances to be subject to the provisos that day allowance is not to be paid in respect of any period spent at a hospital as part of the normal duties of the officer; that night allowance is not to be paid in respect of any period during which accommodation is provided without charge at a hospital; and that day allowance is not to be paid for any period during which subsistence is provided without charge at a hospital.

Any meals taken by an officer at a hospital in the course of his normal duties to be charged for.

Postage

Boards to reimburse any expenditure necessarily incurred by an officer on postage or telephone calls in the service of the board, through the periodical claim for travelling and subsistence.

Digitized by Google

STUDY LEAVE, CONFERENCES, &c.

"Study leave" to be granted in accordance with the following provisional scheme, which is subject to reconsideration.

General Rules

Study leave must be for the purposes of study (including research), teaching, examining, taking examinations, visiting clinics, or attending meetings or conferences of a wholly scientific or clinical character. Where its purpose is to enable the officer to undertake work for which he will receive fees (e.g., teaching and examining) it should normally be without pay or expenses. Where it is granted with pay the officer must not undertake any remunerative work without the special permission of the leave-granting authority.

Study leave cannot be claimed as a right. It can be added to periods of ordinary leave.

A. *For periods not exceeding 7 days.* (Normally such leave would be granted for periods of 1 or 2 days, but in exceptional cases up to 7 days may be granted.)

1. Without pay or expenses—at the discretion of the hospital management committee or board of governors.

2. With pay but without expenses—at the discretion of the regional hospital board or board of governors, though authority may be delegated to a hospital management committee.

3. With pay and expenses—at the discretion of the regional hospital board or board of governors, subject to the rules governing the payment of expenses.

B. *For periods exceeding 7 days but not exceeding 13 weeks.*

1. Without pay or expenses—at the discretion of the regional hospital board or board of governors.

2. With pay but without expenses—at the discretion of the regional hospital board or board of governors.

Any period of such study leave in excess of 3 weeks will involve a surrender of one day ordinary leave for every additional day of study leave granted—e.g., an absence of 5 weeks will involve the surrender of one week's ordinary leave; a period of 9 weeks' leave will involve the surrender of 3 weeks' ordinary leave. For this purpose ordinary leave, not exceeding 3 weeks in all, may be carried forward from the immediately preceding leave year.

3. With pay and expenses—at the discretion of the regional hospital board or board of governors, subject to the foregoing and the rules governing the payment of expenses.

Not more than one period of leave under B 2 or 3 may be granted to one officer in any one leave year. Where an officer is employed by more than one board the leave must be approved by all the boards concerned.

C. *For periods exceeding 13 weeks.*

1. Without pay or expenses—at the discretion of the regional hospital board or board of governors.

2. With pay but without expenses } to be referred to
3. With pay and expenses } Ministry for decision.

Payment of Expenses

1. Where officers are teaching, examining, attending meetings or conferences or visiting clinics, &c., at the instruction of the regional hospital board or board of governors, no question of study leave arises, and expenses will be paid in the usual way and at the usual rates. Expenses in connexion with taking examinations (fees, travelling, subsistence) will not be paid.

2. Where officers have applied for study leave with pay for any of the normal reasons and the board is of opinion that the leave is of advantage to the service, the cost of travelling and/or subsistence may be defrayed wholly or in part at the usual rates.

3. While it is desired to give regional hospital boards and boards of governors the maximum amount of discretion in the granting of study leave, it is nevertheless necessary to obtain a fairly uniform policy in the matter of defraying expenses. For this purpose boards should limit their annual expenditure within the budgets already approved under both heads (i.e., 1 and 2) as follows:

Undergraduate Teaching Hospitals—£800–1200, according to size and circumstances.

Postgraduate Teaching Hospitals—up to £1200, according to size and circumstances.

Regional Hospital Boards (including hospital management committees in the region)—(*a*) Oxford and Cambridge, £1200; (*b*) Newcastle, Leeds, Sheffield, Liverpool, Bristol, and Wales, £1600; (*c*) Metropolitan regions, Manchester, and Birmingham, £2000.

Where the expenditure of a board for 1949–50 is likely to exceed the total stated, and it is not possible to meet the additional cost from "free moneys" at the disposal of the board, application should be made for permission to increase the amount allocated within the budget for these purposes. Regional hospital boards and boards of governors may combine to defray the total or part cost of an officer's travelling or other expenses.

MEDICAL EXAMINATION ON APPOINTMENT

The passing of a medical examination to be a condition of appointment of all officers within the scope of the National Health Service Superannuation Scheme, other than those who are transferred under the National Health Service Act. The examining doctor to be asked to certify that the candidate is "free from any physical defect or disease which now impairs his capacity satisfactorily to undertake the duties of the post for which he is a candidate."

STREPTOMYCIN IN BRITAIN

PRESENT ARRANGEMENTS

THE following statement of the conditions for which the issue of streptomycin is authorised has been issued at the request of the Ministry of Health.

Control of the use of streptomycin is still considered necessary in view of the severe and sometimes permanent toxic effects to which it may give rise. It should, therefore, only be used in conditions where experience has shown that it provides valuable aid, and even then careful dosage is essential. It is also necessary, before beginning treatment, and during its course, to keep a constant watch for the emergence of streptomycin-resistant strains, which may occur with great rapidity. For details of dosage reference should be made to the report of the Ministry's standing advisory committee on tuberculosis.[1]

TUBERCULOSIS

1. *Tuberculous meningitis.*
2. *Acute miliary tuberculosis.*
3. *Tracheobronchial, laryngeal, and pharyngeal tuberculosis.*
4. *Certain types of pulmonary tuberculosis.*

(*a*) Pulmonary tuberculosis in which the lesion requiring treatment is of recent development, is progressive, and is unlikely to benefit from conventional methods (e.g., bed rest and/or collapse therapy) alone. The definition would *include* rapidly advancing pulmonary tuberculosis, in which immediate collapse therapy would be dangerous or impracticable, and acute "spreads," including those after collapse therapy (e.g., postoperative spreads after thoracoplasty). The definition would *exclude* old chronic fibroid or fibrocaseous lesions, apparently terminal conditions, and primary foci or minimal early lesions with favourable prognosis.

(*b*) Pulmonary tuberculosis submitted to lung resection.

5. *Tuberculous wound infections after chest surgery.*
6. *Other sinuses and cutaneous fistulæ of tuberculous origin.*
7. *Abdominal tuberculosis*, including tuberculous peritonitis and tuberculosis of the alimentary tract, except where such conditions are terminal events.

1. *Lancet*, Feb. 12, p. 273.

Digitized by Google

8. *Genito-urinary tuberculosis.**

(*a*) A minimal renal lesion for which nephrectomy is considered unnecessarily drastic until conservative treatment has been tried.

(*b*) Where, after nephrectomy, the remaining kidney is known to be diseased but is not so grossly damaged that cure is considered impossible.

(*c*) Where, after nephrectomy, there is tuberculous cystitis but the remaining kidney is healthy or little damaged.

(*d*) Tuberculous cystitis of any origin (not only that given in [*c*] above) when accompanied by severe symptoms.

(*e*) Some cases of genital tuberculosis.

NON-TUBERCULOUS INFECTIONS

All non-tuberculous infections due to streptomycin-sensitive, penicillin- and sulphonamide-insensitive, organisms (not only meningitis and septicæmia due to such organisms, as heretofore). It is essential that both diagnosis and treatment should be bacteriologically controlled in every instance. Treatment of non-tuberculous infections is of short duration (usually less than a week) and the amount of streptomycin used for each case is therefore very small. It is usual to supply 10 g. for a case in the first instance. Streptomycin has not proved effective in the treatment of enteric fever and bacterial endocarditis.

The following points should be kept in mind:

Non-tuberculous Genito-urinary Infections

(*a*) The common infections are due to *B. coli*, *Ps. pyocyanea*, and *Proteus*. In past series the infection has been controlled in about half the cases; in the remainder the organism has become resistant, or resistant secondary invaders have appeared.

(*b*) Control of the infection or the development of resistant organisms usually occurs within 48 hours of starting streptomycin.

(*c*) The treatment is contra-indicated in patients with some underlying conditions—e.g., obstruction, calculus, tuberculous infection. In such instances relapses are almost invariable after withdrawing streptomycin.

(*d*) The treatment recommended is 3 g. streptomycin daily in four doses for 48–72 hours. The urine should be cultured daily and organisms tested for streptomycin sensitivity.

Influenzal Meningitis

The most effective treatment for influenzal meningitis is still under investigation by the streptomycin clinical trials (non-tuberculous conditions) committee of the Medical Research Council, and it is urged that doctors having apparently suitable cases should, in the first instance, seek the advice of the nearest Medical Research Council centre.

The following is a list of the present Medical Research Council centres for the investigation of the effects of streptomycin treatment in non-tuberculous conditions:

Sir ALEXANDER FLEMING, Inoculation Department, St. Mary's Hospital, W.2.
Prof. R. V. CHRISTIE, Dunn Laboratory, St. Bartholomew's Hospital, E.C.1.
Prof. CLIFFORD WILSON, Medical Unit, London Hospital, E.1.
Dr. F. R. SELBIE, Bland-Sutton Institute of Pathology, Middlesex Hospital, W.1.
Prof. A. W. DOWNIE, Department of Bacteriology, School of Hygiene, Mount Pleasant, Liverpool, 3.
Prof. R. W. B. ELLIS, University Department of Child Life and Health, 19, Chalmers Street, Edinburgh, 3.
Dr. A. L. P. PEENEY, Queen Elizabeth Hospital, Birmingham.
Prof. C. H. STUART-HARRIS, University Department of Medicine, the Royal Hospital, Sheffield, 1.
Prof. H. B. MAITLAND, Department of Bacteriology and Preventive Medicine, Public Health Laboratory, York Place, Manchester, 13.
Prof. STANLEY GRAHAM, Royal Hospital for Sick Children, Glasgow.
Prof. J. W. MCLEOD, Department of Bacteriology, the School of Medicine, Leeds, 2.
Dr. N. C. GRAHAM, Institute of Pathology, Grosvenor Road, Belfast.
Prof. ALAN MONCRIEFF, the Hospital for Sick Children, Great Ormond Street, W.C.1.
Sir LIONEL WHITBY, Department of Medicine, University of Cambridge.
Sir HUGH CAIRNS, the Radcliffe Infirmary, Oxford.
Dr. R. H. DOBBS, Queen Elizabeth Hospital for Children, Hackney Road, E.2.

* The treatment of this category is at present limited to certain centres, the names of which may be obtained from regional hospital boards.

In England Now

A Running Commentary by Peripatetic Correspondents

FROM the well-nigh perpetual occupation of seeing Mr. Bevan's patients many of us, I fancy, are busy seeking respites. One of mine is road-building. It is not a very posh road—tiddn a turnpike azackly—nor is the job particularly skilled. It consists merely in spreading dumped lorry loads of brick and rubble and covering them with clinker ready for the steam roller; but it is comforting and honest toil. Three of us get down and lend a hand whenever we can, but George is on the job full time.

Proper chap is George. Seventy-two and square built, he just goes on and on and on. You have to tell him when it is time to knock off, otherwise he would work all night and all the next day without noticing. Nobody could call him garrulous. Before giving utterance he ponders carefully, and a remark rolls off the assembly line perhaps twice an hour. When it comes it is generally humorous, often of an Elizabethan bawdiness, and delivered, except for the wicked twinkle in the eye, with a wooden impassivity of face. Served in two wars George has. He enjoyed the South African job which he says were a nice trip, but in the Fourteen Affair he was an infantryman and there was too much of this yur diggin' even for him; and that, you may be sure, means a lot. His habit of working steadily without looking at the clock rather dates him, and so do some of his pronouncements. To help in our task one of us produced a new shovel—a scoop, as we call it. It is a very fine shovel but rather an outsize affair, only to be lifted with difficulty even when unloaded. While the rest of us stood round in respectful silence George took it up and examined it carefully, feeling and handling it like the maestro he is. He grunted non-committally and began to shovel. "Twaddn niver made for no *white* man," he said. But we can't get it away from him. Proper chap is George.

* * *

I have recently taken over a ward in a London hospital and have been struck by the extent to which patients are subjected to investigation and treatment. One woman of 69, suffering from long-standing postprandial epigastric pain and mild hypertension, having exhausted the local facilities for investigation, was transferred to another hospital for gastroscopy. On her return I asked her how she was feeling. Wreathed in smiles, she replied, "Much better, thank you." I then asked the nurse what treatment she had been having. On hearing the following list of drugs I was not surprised that the old lady was feeling better without them.

Tab. phenobarbitone gr. ½ b.i.d.
Thyroid extract gr. ½ b.i.d.
Dienœstrol 4 mg. b.i.d.
Acid hydrochlor. dil. min. 30 t.i.d.
Penicillin 300,000 units 3-hrly.
Mist. pot. cit. 1 oz. t.i.d.
Mist. pot. brom. 1 oz. nocte.
Charcoal biscuits as required.

Three other drugs had been crossed off the list during her short stay in hospital. I requested that all the others might be crossed off so that we might start afresh. Next day the patient said she was so glad that she did not have to go on taking all these medicines. The improvement has been maintained.

* * *

The use of kitchen scales for weighing always calls for individual technique. Ours have a negative reading of 6–8 ounces which must be allowed for. I was posting my medical books back to my lodgings, laboriously packed in two ex-canned-meat boxes, with winter pants and vests rammed in to steady their contents. At last I struggled along to the post-office with them. The assistant behind the counter hardly looked up from her knitting, even when I hoisted the first parcel on to the scales, so I coughed, loudly and without regard to the advice of the Central Council for Health Education. "Sorry, 's overweight," said the P.M.G.'s respresentative. "Two ounces." "Oh," said I, "is this one all right?" heaving up the second parcel. "Yep, that's just right.

Digitized by Google

But it won't go now. Leave it at your own risk overnight." Thoughts of the crime wave entering the sub-post-office and washing away Rose and Carless, Romanis and Mitchiner, Handfield-Jones and Porritt, Bailey and Love, all at once, at dead of night, so chastened me that I meekly gathered up both parcels, despite protests from biceps and flexors.

At home, suitable adjustments of the kitchen scales showed that the mere dropping of Haultain and Kennedy would satisfy the requirements of the Postmaster General as to weight; so off I went again, this time to a branch office. "Sorry," said the clerk. "We're closed for parcels."

* * *

Cautionary Tale.—George Bulmer Ditherby was a medical student with High Principles. Otherwise he might have reached the shady side of Harley Street. In his clinical examination for the M.B. it never occurred to him to bribe the Case. Yet a Case when bribed may reveal the diagnosis. So G. B. Ditherby, who might have become Sir George Bulmer Ditherby, is now managing a cinema on the Gold Coast.

It happened thus. When Mr. Ditherby, as he was and is, approached the Case there were two half-crowns on the top of the locker beside the bed. The idea of bribery never entered his mind; and he sought to obtain the history of the Case. The Case, a fat, florid man, was not coöperative. In reply to a leading question, he admitted there had been a sharp pain on the right side—"Stitch in the ribs, that's wot it was." Mr. Ditherby knew better. The Case also admitted shortness of breath. Inspection revealed an obese man with spare tyres round his middle. Strong percussion made the right thorax hyper-resonant. Breath sounds were not audible. In fact, nothing was audible. Deep palpation found the apex beat in the left midaxillary line. Mr. Ditherby awaited the examiner.

His examiner was a pleasant middle-aged man who believed in helping the candidate. (The candidate of today is the doctor of tomorrow: a doctor may need a consultant.) "Well, Mr. Ditherby," he said, "and what do you make of this case?" "Spontaneous pneumothorax, Sir. Probably due to a bulla, because he doesn't look like tuberculosis."

Ex.: "Let's talk it over. What symptoms and signs did you find?"

Dith.: "Acute pain in right side followed by dyspnœa and cyanosis. Right thorax hyper-resonant. Absence of respiratory murmur. Being single-handed I was unable to get the bell sound. But if you would be so kind, Sir, as to tap the half-crowns while I listen—I mean auscultate—I . . ."

Ex.: "No, no, we won't bother about that. Incidentally, that sign is not always present. Did you examine the heart?"

Dith.: "Yes, Sir. The apex beat is in the left midaxillary line."

Ex.: "Quite right. What does that suggest?"

Dith.: "Displacement of the mediastinum."

Ex.: "That would be a considerable displacement. What about the heart sounds?"

Dith.: "N.A.D., Sir, I mean nothing abnormal detected." The Case snorted.

Ex.: "Between you and me it's difficult to get physical signs in obese subjects. Well do I know it. I'm sorry but this is a cardiac case—mitral and aortic. Never mind, Ditherby, better luck next time. We all make mistakes."

The examiner was really sorry for Ditherby, and was also a little puzzled. The two previous candidates, stupid looking fellows, had diagnosed the case without difficulty.

Moral.—There are better uses for half-crowns than producing bell sounds.

* * *

The Swedes have a charming habit of unconsciously dropping English faux pas at unexpected moments. It was a lovely afternoon when we arrived in Uppsala, and gazed up at the 14th century Gothic cathedral. Explaining the programme our guide concluded: ". . . and when we have finished I guess we go round si backside and meet my friend, si Archbishop." Ever since, in our thoracic surgery clinic, when we turn the lung over to dissect the inferior pulmonary vein, the remark floats up—"and now to meet si Archbishop."

Letters to the Editor

OBJECTS OF RESEARCH

SIR,—In attacking the suggestion that geriatrics should be recognised as a specialty, Dr. Ellman (Feb. 12) invokes those hoary shibboleths—the dangers of ultra-specialisation, compartmentalism, artificial divisions, and the rest. It is not clear where he draws the line between specialisation and ultraspecialisation, or whether he is opposed to specialisation except when practised by physicians with specialised leanings, though it would seem that he does object to the development of new specialties.

I have no personal interest in geriatrics as a specialty, and indeed regard age as the least defensible basis for a specialty; but I am concerned that in principle new specialties should be encouraged, for as has often been said, they are the growing-points of medicine. Unless a culture grows it must wither and die. As I see it, specialisation is merely an expedient for increasing knowledge. It is a valuable instrument for this purpose; as Fraser remarks in *The Golden Bough*, it is mainly by specialisation that man has raised himself above the level of the savage. Differentiation of function is a biological and practical necessity. To attempt to prevent it is to court disaster.

The contributions of general physicians to medicine have indeed been great; but nowhere is knowledge so complete that we can afford to ignore, or to suppress, the contributions that those who wish to undertake more intensive study may have to offer. What Dr. Ellman refers to as departmentalism and artificial divisions are temporary but necessary devices for securing better facilities for more intensive study. Properly used they are the reverse of harmful.

There is little likelihood in my view that anyone who specialises seriously will fail "to cling fast to the foundations of medicine." He cannot do otherwise, for in no branch of medicine can one more than scratch the surface without at once being confronted and confounded by the most recondite problems in science. Compartmentalism breaks down a very little way below the surface, but on the surface it has its uses.

I see no danger in specialisation though much in its abuse, and little danger in the multiplication of specialties, since those that prove redundant will soon disappear. There are of course many who, like Dr. Ellman, sincerely believe that the multiplication of specialties is a menace. Their sincerity commands our respect though we may disagree. Unfortunately there are also some—and they are not few—who exploit this doctrine for professional and personal ends. To my mind the constant reiteration of the alleged dangers of specialisation, by affording a pretext for the unscrupulous, is a greater menace.

London, W.1. A. A. OSMAN.

LYMPHOCYTES AND INTRAVASCULAR HÆMOLYSIS

SIR,—I read with interest Dr. Trinick's preliminary communication in your issue of Feb. 5. Leaving aside the question of gamma-globulin production, the morphological appearance of the cells he describes is possibly open to other interpretation than that of a specific mechanism for detachment of cytoplasmic masses.

In the course of research on the blood-cells of lower vertebrates, chiefly fishes, I have observed similar bud-like cytoplasmic outgrowths of lymphocytes, and also of other blood leucocytes. The blood leucocytes of fishes survive for longer periods than those of mammals when examined in isotonic-saline media, permitting clear observation of their activities. In freshly made suspensions of blood in saline, examined in hanging drops at room temperature, lymphocytes appear as translucent, faintly granular bodies with a smooth outline devoid of any suggestion of cytoplasmic outgrowths; and the granular leucocytes display active amœboid movements, taking up a variety of different shapes, and adhering to the under-surface of the cover-slip. If the preparation is allowed to stand for half an hour, and then re-examined, the leucocytes present a very different appearance, both granular and lymphoid cells now floating freely

Digitized by Google

in the saline, the former having adopted a spherical outline and no longer showing any activity. Both granular leucocytes and lymphocytes are seen to have developed small balloon-like protrusions from the cell surface; these protrusions are perfectly translucent and devoid of all granules. It seems reasonable to suppose that we are dealing here with cells which are dead or dying, the cell-membrane losing its differentially permeable character in these localised regions, so that water rapidly enters the cytoplasm and inflates the membrane to form these observed protrusions. Similar protrusions are seen in dying protozoans, as in amœba and paramecium. I have also observed them frequently in lymphocytes in smears of fish blood treated with Leishman's stain-fixative in the usual way, but not in granular leucocytes in the same smear preparations.

There is thus a strong possibility that Dr. Trinick has been dealing with a normally occurring artefact in his preparations. The question might well be resolved by an examination of freshly drawn blood in a hanging-drop preparation on the warm stage, so that the appearance of a living lymphocyte could be observed in conditions as near normal as possible.

Medical School, King's College, Newcastle-on-Tyne. W. T. CATTON Lecturer in Physiology.

SHEFFIELD REGISTRARS' GROUP

SIR,—I should like to announce through your columns that a United Sheffield Hospitals Registrars' Group was formed here on Feb. 4. The group has received the official recognition and the encouragement of the United Sheffield Hospitals medical committee.

Royal Infirmary, Sheffield. R. S. WEETCH Secretary, executive committee.

MANAGEMENT OF PEPTIC ULCER

SIR,—In your leading article of Feb. 26, you speak of a growing body of opinion that the regimen usual for ulcer patients is too rigid. You stress the shortcomings of medical treatment, the tediousness and impracticability these days of drastic dieting, the failures of surgical intervention, and the boomerang tendency of prolonged rest and other over-restrictive régimes. Rightly you opine that it is mental rather than physical rest that is important, and you make a passing reference to the frustrations besetting the restless, eager, and ambitious personalities constituting so many of the ulcer-bearing patients.

Many authors have drawn attention to the underlying personalities of these patients; A. T. M. Wilson in this country, and Wolff, Bolen, Draper, and Katz in America, have all stressed factors of anxiety, frustration, hostility, and resentment acting on hypersensitive and hyperactive people, causing the inward direction of strong emotional stimuli. The psychosomatic theory has been reinforced both by psychoanalytic explanation and by the observations of Wolff and Wolff on the mucous membrane of the human stomach in the presence of certain emotional reactions; and others have shown how hypermotility and hyperactivity are evoked by, and recede with, the presence and the absence of anxiety, rage, and other moods.

This is not to claim that the emotional side of all chronic peptic-ulcer patients is always the most important, or the most amenable to treatment. Like so many psychosomatic disorders, sequences rather than causes must be sought. The language of symptoms and the end-results we recognise as disease entities are limited; but there is a multiplicity of factors, constitutional and environmental, that may comprise an ætiology. Suffice to say that there appears to be a close connexion between the psychic side and the gastric function. Wilson goes so far as to remark that "since psychiatric treatment is probably directed to the basic disturbance it may possibly prove more successful in the end."

There is, I think, enough evidence now to justify a careful examination of all such patients (and certainly young ones) for psychogenic factors. A careful psychosomatic history, and an assessment of personality type and of possible operating factors such as anxiety and frustration, should be followed by psychosomatic explanation and efforts to readjust environmental and social influences, over-ambitious aims, and other reaction phenomena. Dieting, frequent small meals, sedation with phenobarbitone, and the use of alkalis with atropine, are all useful at times. But the therapeutic value of rest and sedation should be used only to relax and soothe the body-mind—not to hide and cloak the underlying discontent of the psyche, so leaving the patient still stewing in his own gastric juice.

I recall a woman, aged 48, who had survived three severe hæmatemeses from a chronic gastric ulcer. She was finally persuaded to accept a long and careful medical treatment, after which a consultant of international standing was able to pronounce the ulcer completely healed. That same evening she had another and grave hæmorrhage, a few hours after hearing some very disturbing family news.

The juxtaposition of the emotional life-history of the patient and his symptoms will often make more sense than their attempted association with dietary transgressions or other physical incidents.

I cannot agree that even in the chronic cases there should be "an acceptance of the inevitable," or that the patient should "come to terms with his disability." A young South African who had had asthma all her life came to London for advice, and after examination by chest physician, allergist, and bacteriologist, she was gravely told by them in consultation that she "should learn to live with her disability." It is satisfactory to be able to report that she did not take this consolatory and defeatist advice. She was able to return home after having "learnt to live without her asthma." May not this positive approach have its rôle too in the elucidation of that body-mind disorder we recognise as peptic ulceration? To the two lines of your old song I should add:

I cannot eat but little meat,
My stomach is not good;
The pain I get and oft repeat
Depends upon my mood.
I've always had a strong conceit,
I cannot tolerate defeat,
It all dates back to mother's teat,
And acids all my food.

London, W.1. S. CHARLES LEWSEN.

HEALTH CENTRES NOW?

SIR,—Your article of Feb. 26 in the Act in Action series and "Practitioner's" letter of March 5, both seem to imply that the one thing necessary to ensure smooth operation of the Act is improved waiting-room accommodation.

"Practitioner" mentions the 3-hour wait the patient may have. But what of the doctor? This overworked and underpaid menial will have two surgeries of this length, and some time in between he has to manage all his visits. To do anything to attract more patients will result in the 3-hour surgery lasting for 4 or 5 hours, with a resultant further deterioration in the standard of the work done; for a tired man cannot do good work.

Let us have some sense of proportion—at present sadly lacking in Governmental circles—about this health service. As Dr. Ffrangcon Roberts has said, the potential demand for medical treatment is unlimited. Therefore there must be either an unlimited supply of doctors (which there is not and which in any case the country could not afford) or there must be a deterrent. In the past, financial considerations have been a very satisfactory deterrent. Now the only safeguard is the limited capacity of the waiting-room. If this last remaining bulwark against inundation by those who like something for nothing is removed, the service will break down completely. True, it causes hardship in some cases; but a general breakdown in the service would cause more.

There is one remedy—more satisfactory than any hurried creation of health centres. Let the patient make a token payment at each attendance. Queues will disappear by the elimination of trivialities. The doctor will have time to treat patients with reasonable care and, lastly, he will have the satisfaction of earning in 10–12 hours *nearly* as much as the optician earns in 6.

Silver End, Essex. J. W. NICHOLAS.

Digitized by Google

HODGKIN'S DISEASE

SIR,—Your leading article of March 5 again emphasises the fact—recognised fully by pathologists but not so fully by clinicians—that Hodgkin's disease affects the whole reticulo-endothelial system.

The technique of deep X-ray therapy used by Mr. T. Anthony Green is based on recognition of the pathological picture. Since radiotherapy can only be palliative, intense local treatment to a mass of glands, with severe resultant reactions, is not justified; for lower dosage can achieve the same symptomatic result. The technique adopted in this department (equally effective in other reticuloses, such as the leukæmias) is as follows:

The symptom-producing mass of glands is treated first, using a dosage of approximately 500r tissue in one week, blood-counts being performed before and after treatment. If the patient's condition is satisfactory, the remainder of the body from neck to groins is then treated in strips, the method being referred to as the "step-ladder" technique. Two fields 30 × 12 cm., one anterior and the other posterior, are used to give a dose of 300–500r in one week per strip according to the patient's condition. The blood-count is recorded weekly and whenever possible the strips are treated in consecutive weeks until the whole neck and trunk have been covered. If the patient's condition is poor or the leucocyte-count has dropped significantly, the course can be interrupted at any strip.

By this means an effective dose (which cannot be achieved by the body-bath method) is given to the patient without any severe constitutional effects. It gives long periods of remission without precluding further treatment when required.

R. F. HENDTLASS.

Radiotherapy Department, Royal Northern Hospital and Prince of Wales's General Hospital, London.

PRACTICE OUTSIDE THE SERVICE

SIR,—Would your peripatetic correspondent of two weeks back please give us some grounds for his assumption that the N.H.S. patient who needs 45 minutes of his doctor's individual attention does not, in fact, get it? It seems rather a serious statement to make without the support of direct evidence. I would assure him that the only unhurried thing still left in a doctor's life *is* the examination of the patient and any discussion that may arise from it—in sickness or in health. This is not the occasion for economising in time.

If your correspondent is anxious to reassure himself on this point, I suggest that he ask the patients themselves. I can put him in touch with random selections of our N.H.S. patients representing every income-group from zero to four figures; I feel sure that they would all have something helpful to say about the National Health Service. Armed with such first-hand evidence from people who have personally "suffered" the service, he would be assured of a respectful hearing from us "insiders."

Bagshot. S. GRAHAM.

VEGANIN

SIR,—In his letter of March 5 Professor Alstead agrees that 'Veganin' tablets disintegrate in water and in gastric juice more rapidly than do tab. codein co. (whereas 'Veganin' tablets disintegrate in 20 seconds or less, we have reports of failure of tab. codein. co. to do so in 24 hours); but he claims that this is unimportant, because the tablets should be pulverised. My information is that patients do *not* pulverise analgesic tablets. I can assure him that the solubility of the active ingredients in 'Veganin' is at least equal to that of those in any tab. codein. co.

I would not presume to argue with a professor of pharmacology as to whether a simple addition of the weights of active ingredients decides the effectiveness of an analgesic tablet, irrespective of the balance of the formula, the quality of the ingredients, and the skill and care exercised in production; but the view of practising physicians who have been observing the results for some years may be accepted as evidence. There seem to be very few who use tab. codein. co. in preference to 'Veganin' for themselves and their own families, nor many who would do so for their paying patients; and since the Minister of Health stated clearly that prescriptions under N.H.S. must be for the most effective medicines, practitioners are increasingly prescribing 'Veganin' under N.H.S. too.

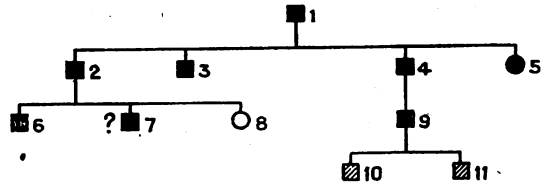
My "indignation," to which Professor Alstead refers, was directed to the misuse of our trade-mark 'Veganin,' which misleads patients into believing that the effects, or otherwise, of anonymous tab. codein. co. are attributable to our product. The professor teaches his pupils that tab. codein. co. are as good; we trust that he will warn them that these should not masquerade as 'Veganin,' either in hospitals or elsewhere.

The price per 100 quoted by Professor Alstead includes purchase-tax, which will not be chargeable on dispensing packs after May 2, and, so far as N.H.S. is concerned, is only a transfer from one Government pocket to another meanwhile.

William R. Warner & Co. Ltd., London, W.4. ELIOT WARBURTON.

PEPTIC DISORDERS IN A FAMILY

SIR,—The occurrence of gastric and duodenal disorders in succeeding generations of a single family is indicated by the accompanying figure. The following is a summary of the patients' histories: (1) died, aged 72, of cancer of the stomach; (2) died, aged 71, of cancer of the stomach; (3) operation for cancer of the stomach, still living, aged 68; (4) died, aged 66, after operation for



Symbols (square = male, circle = female): black = gastric carcinoma, stippled = duodenal ulcer, unshaded = gastric ulcer.

cancer of the stomach; (5) died in hospital, aged 63, of cancer of the stomach; (6) died of cancer of the stomach; (7) ? cancer of stomach, still living, aged 71; (8) died in hospital of gastric ulcer; (9) operation when aged 67 for cancer of the stomach, still living, aged 75; (10) duodenal ulcer when aged 39, still living, aged 45; (11) operation for duodenal ulcer when aged 44, still living, aged 48.

The 75-year-old man and his two sons have been patients of mine for the past ten years.

Rayleigh, Essex. C. H. BATEMAN.

THE CUTS

SIR,—The diagnosis of the financial situation presented in last week's leading article lacks some of the history of the case and so may fail to provide a satisfactory basis for treatment. It dates not from the appointed day but from the assurance given by the Coalition Government to the voluntary hospitals that their work should not suffer through lack of funds. Added to that was the extraordinarily generous method of payment for beds to be available for emergencies. The first gave the voluntary hospitals a sense of financial security such as they had never known before. The second provided them with funds on a large scale so that bank overdrafts disappeared to a quite remarkable extent before the end of the war. Unlike the municipal hospitals the "voluntaries" knew no kind of budgetary control, with the result that, led by the teaching hospitals, they indulged in a financial debauch of which they are now feeling the after-effects. Months before the appointed day the more sober-minded realised that indulgence on that scale was bound to be followed by headaches.

To the suggestion that there must be in the background some system of checking the comparative costs, the simple answer is "take the figures for 1938 and add a reasonable percentage." Even if it is the fancy figure of 185% suggested last week in another connexion (p. 446), it will be interesting to see to what extent the accounts for 1948 exceed it.

LONDONER.

Digitized by Google

DIABETES

SIR,—In your issue of Feb. 5 "Medical Officer of Health" suggests that "every diabetic, however mild, should receive insulin." Few, I think, would agree with him. He then goes on to state that his only complications have been hypoglycæmic attacks, one of which was "provisionally diagnosed" as diabetic coma, for which he was given insulin "pending a blood-sugar estimation."

I do not doubt that the casualty officer or R.M.O. responsible for this unfortunate therapeutic effort thought he was doing the proper thing; but how can even a "provisional diagnosis" of diabetic coma be made in a patient who became suddenly unconscious? Diabetic coma is never of sudden onset; and one has to assume that, as the episode occurred at a medical meeting, a reasonably accurate history was available. It has been the fashion to make light of the dangers of hypoglycæmia, some even holding that death from hypoglycæmia is a clinical curiosity; but recovery from insulin coma may be accompanied by potentially dangerous complications, especially cerebral.

Whereas one can do no harm by the intravenous injection of 30–40 ml. of 50% dextrose into a patient in diabetic coma, one can kill or seriously injure a hypoglycæmic patient by giving him more insulin. And why wait for a blood-sugar estimation? Diabetic coma is due to ketosis and is not the direct result of hyperglycæmia; a catheter specimen of urine is easily and quickly obtained, and if it contains no acetone the coma cannot be diabetic.

I feel that more time could profitably be spent in teaching our senior medical students the differential diagnosis of coma (diabetic or otherwise) and in impressing on them the fact that unconsciousness in a known diabetic patient may be due to causes other than ketosis.

Birkenhead Municipal Hospital. J. L. BLAIR.

POSTURE FOR LIVER BIOPSY

SIR,—The chief danger of needle biopsy of the liver is hæmorrhage, which is sometimes caused by the patient's moving. The patient is usually told to hold his breath while the biopsy is being taken, but sometimes he cannot do so properly throughout the operation. This difficulty can be overcome by adopting the following procedure. The patient sits upright in bed with his knees drawn up and leans forward as far as possible. Radioscopy of 15 patients has shown that in this position there is no respiratory excursion of the lower border of the right lung, and the adjacent posterior part of the diaphragm becomes almost, if not quite, motionless, thus immobilising the liver and making it possible to do the needling easily and without any need for haste. Naturally, care should still be taken to insert the needle only at a site where percussion indicates the absence of intervening intestine. This is usually found between the scapular and posterior axillary lines. If such a site cannot be found, biopsy must be postponed. This method is unsuitable for dyspnœic patients.

Budapest. EMERY SCHILL.

HÆMOGLOBINURIA

SIR,—I believe that Stats, Wasserman, and Rosenthal,[1] whose experience is quoted in your leading article last week, are unnecessarily cautious in recommending that blood-transfusions given to patients suffering from paroxysmal nocturnal hæmoglobinuria should be kept to a minimum. In this disease it seems that the transfused plasma rather than the erythrocytes causes the reactions and exacerbations of hæmolysis that are sometimes observed. If the corpuscles are freed, or almost freed, from plasma by washing the blood with saline before transfusion, reactions appear to be abolished.

I have two patients suffering from this disease who without transfusions become incapacitated by a serious degree of anæmia (erythrocyte-counts about 1,500,000 per c.mm.). For more than a year they have been treated as outpatients, at approximately six-week intervals, with transfusions of the washed erythrocytes derived from 2 pints of blood; and in this way their erythrocyte-counts and hæmoglobins have been maintained at levels allowing them to lead fairly normal lives. In no instance have there been reactions when washed corpuscles have been transfused, and they have travelled home by bus or tube to the other side of London within 30–60 minutes of the transfusions being completed.

Hæmoglobinuria has sometimes, but not always, been abolished by these relatively small transfusions. However, if larger volumes are transfused and the patient's blood-count raised more nearly to the normal level, striking temporary remissions may be obtained.[2]

Finally, two small points in relation to diagnosis. Firstly, the heat-resistance test of Hegglin and Maier,[3] although a useful pointer to a hæmolytic anæmia, is non-specific; quite rapid spontaneous hæmolysis may be observed in other types of severe hæmolytic anæmia. Secondly, Ham's test is better described as an acidified-serum hæmolysis test—not as an acid hæmolysis test. It is not a question of the sensitivity of corpuscles to acid; acid is added to serum before the addition of the suspension of corpuscles only to adjust the pH to the optimum (about 7·0) for the action of the serum factors.

Department of Pathology, Postgraduate Medical School of London. J. V. DACIE.

BACTERIAL WARFARE

SIR,—Your leading article of March 5 provoked thoughts, more widely shared perhaps than expressed, on the identity of aim between old-time magic and modern science. Both propose to learn the "know-how" of the forces of nature, to compel them to serve human ends. As there was a white magic, so there is what may be called a white science, when the powers thus made available are harnessed for human good. But science, like magic before it, is all too prone to be seduced to evil uses.

When in difficulties, the masters of the totalitarian states of the past, the Babylonian and New Egyptian empires, summoned their sorcerers and magicians in the same way as their successors of today call upon the scientists. There is no reason to suppose that modern successors to Daniel and Moses will be lacking to put to rout this improper use of science by an appeal to higher Authority; and considerations such as you have raised do suggest that the medieval idea of the subordination and coördination of all sciences under theology, their queen, may not be as foolish a notion as it may have appeared fifty or a hundred years ago.

Darlington. JOSEPH V. WALKER.

INHALATION OF STOMACH CONTENTS

SIR,—Dr. Willcox's case-histories of inhaled stomach contents during anæsthesia for operative interference of labour, are most interesting and valuable. His warning against a full stomach can be extended to include all cases where the patient feels himself incapable of making a satisfactory reaction to the pressure of painful events.

It is premature to generalise from the beautiful demonstration by A. E. Barclay and F. H. Bentley[4] of arteriovenous shunts under sympathetic control in the gastric submucosa; but it may be that in the stress of anxiety and sympathetic hypertonus an anæmic and functionless mucosa leaves ingested food unchanged and poised for emesis. The traumatised child, bewildered and in pain, is such a subject, as the following cases serve to illustrate.

CASE 1.—A 5-year-old boy received a lacerated scalp while playing three hours after luncheon. Three hours after injury he was anæsthetised with gas and oxygen, and ether. During induction the patient vomited fluid material, some of which he inhaled. Resuscitative measures and bronchoscopy were carried out, but the child died. At post mortem both lungs were congested and the bronchi blocked with food particles.

CASE 2.—A girl of 9 years had lunch at 1 P.M. At 3 P.M. she fell from her pony. She was remounted and rode home

1. Stats, D., Wasserman, L. R., Rosenthal, N. *Amer. J. clin. Path.* 1948, **18**, 757.
2. Dacie, J. V. *Clin. Sci.* 1948, **7**, 65.
3. Hegglin, R., Maier, C. *Amer. J. med. Sci.* 1944, **207**, 624.
4. *Brit. J. Radiol.* 1949, **22**, 61.

Digitized by Google

with a severe supracondylar fracture of the left arm. At 9 P.M. she was anæsthetised with gas and oxygen, and 'Trilene.' During induction she vomited tomato, meat, and solid potato particles. Postural drainage was effective and no vomitus was inhaled.

In attempting to assess the danger of regurgitation during anæsthesia in these cases, the time between the ingestion of food and the onset of the painful occurrence should be taken as the effective digestion time. Thereafter, in the absence of rest and relaxation, the passage of time is no criterion of an emptying stomach; and if an emergency anæsthetic has to be given, the possibility of an artificial evacuation should be considered.

Emsworth, Hants. P. R. BROMAGE.

SIR,—I have read Dr. Willcox's article with considerable interest. I should not agree that inhalation of stomach contents is an unusual accident in these days. It occurs rather too frequently, and the patients are not always fortunate enough to walk out of hospital. I consider that in every case of this kind immediate bronchoscopy and suction should be instituted; it is a life-saving measure. One other point—about Dr. Willcox's 2nd case. Is it not a little unwise to administer thiopentone when one is not certain of an empty stomach? I should like to endorse the opinion that the custom of feeding patients in labour is "risky and should be abandoned."

St. Heller Hospital, Carshalton. HOËL PARRY-PRICE.

A PICTURE SOUGHT

SIR,—A copy of the picture in which Dr. Terence East (Feb. 26) is interested used to hang in the medical outpatient department of King's College Hospital when I was a student there in 1932. The late Dr. A. C. D. Firth used it to impress upon his clerks the importance of the five senses in clinical diagnosis. If, in the course of examining a patient, a clerk had forgotten to look at the tongue and feel the pulse, he was at once sent to look at the picture. It is refreshing to recall those days when diagnoses were made more by clinical acumen than by the filling up of a large number of request forms for intricate investigations.

Aylesbury. RALPH H. GARDINER.

TRICHLORETHYLENE IN LABOUR

SIR,—It is with some hesitation that I enter the controversy over trichlorethylene and its use by midwives,[1] but I have been using 'Trilene' ever since it appeared on the market, for all manner of painful procedures including midwifery. First I employed a modified Clover's apparatus[2]; and since then the 'Cyprane' inhaler, which was kindly lent to me by the makers. The latter is very neat and portable, and has, so far, answered all my requirements in general practice. It does not work on a fixed percentage basis, but it can be locked to give the mixture most suitable for self-induced analgesia for each individual. I do not like fixed-percentage machines and have had no experience of the Freedman.

The Minnitt machines have often proved far from satisfactory. When the first was installed at a county maternity hospital, I offered to give the nursing staff a demonstration of its use.

The first volunteer nurse, seated in a chair, completely lost consciousness after a very short period; but as she was anæmic and rather neurotic I thought that might explain her behaviour, and I proceeded with the second—a buxom type. She too soon began to lose consciousness and I stopped the induction. The third was the sister, a bucolic type with no nonsense about her. She became more deeply anæsthetised than the first, and took much longer to recover consciousness, and her dignity. None removed the finger from the hole, or dropped the facepiece; they first slumped forward, and would have fallen on the floor if I had not prevented it.

After this rather alarming display—for I had previously assured them that anæsthesia was not possible with this machine—I made some inquiries, and was informed that many of those machines had got on to the market wrongly calibrated. Other Minnitt machines erred in the opposite direction in that the percentage of nitrous oxide was too low to give any real relief of severe pain. Is it then, I wonder, possible to produce a foolproof machine that is really satisfactory in, if not all, at any rate a large proportion of cases?

Finally, is the average midwife, who has had some training, less competent to supervise self-induced analgesia than the average unqualified dentist, with no training, is to give full gas-and-oxygen anæsthesia to all manner of persons?

Keighley. WRIGHT LAMBERT.

SIR,—I should like to support the excellent letter of March 5 from Dr. Hopper. I am strongly in favour of his suggestion that an investigation should be carried out in the homes of the patients, to see whether 'Trilene' is really suitable for use by midwives.

New Barnet. JOHN ELAM.

SIR,—The conclusive article of Feb. 26 by Dr. Prescott and his colleagues proves that even the most recent analgesics reduce the sensitivity of the respiratory centre. The article is most timely in view of the proposed issue of analgesia equipment to midwives and the possible subsequent increase in asphyxia neonatorum.

Fortunately, the article shows us a means of counteracting this reduced sensitivity, and of stimulating the respiratory centre. For the experiments the familiar 5% carbon-dioxide and oxygen cylinders were used, as well as a cylinder with only 3% carbon dioxide. The 5% concentrate was twice as potent as the 3%. This coincides with the teaching, ten years ago, of Prof. Yandell Henderson, who observed that in asphyxia neonatorum the respiratory centre was so often desensitised by lack of oxygen that a whiff or two of highly concentrated carbon dioxide (even 30%) was needed to stimulate it. In other words, carbon dioxide is more essential than oxygen; and therefore there is no need for the midwife to carry an oxygen cylinder, for fear of asphyxia due to the analgesic.

My large experience of domiciliary midwives' efficiency today gives me confidence to support the issue to them of analgesics, provided that they also carry a supply of carbon dioxide.

Hemel Hempstead. GILBERT BURNET.

RETROPUBIC PROSTATECTOMY

SIR,—In prostatic surgery I am an unrepentant "punch" resectionist, but I feel that Mr. Millin is to be congratulated on the success of his retropubic operation as described in your issue of March 5. I should like, however, to comment on one of the conclusions which have been drawn.

"Earlier operation should be advised in established prostatic obstruction." This counsel must be interpreted with great care. Enlarged prostates vary greatly in the degree of obstruction which they produce. In the milder degrees the obstruction is overcome by hypertrophy of the bladder, which can be recognised by the appearance of trabeculation on cystoscopic examination. It is my practice to treat expectantly all patients with prostatic enlargement and only a small quantity of residual urine, unless difficulty in micturition is very extreme. Recently I reviewed those patients of this group who had been seen for the first time between 1938 and 1947.

The series included 129 patients. After a period of expectant treatment I have operated on 13 of these patients, and 4 others have had operations by other surgeons. The remainder show no evidence of increasing obstruction; 14 have been followed for over eight years and 49 for over six years. Of the patients examined cystoscopically the majority showed trabeculation of the bladder; in 14 this was pronounced, yet only 1 of these has had a progressive course. Of these 14, 4 have been followed for about five years; 1 now has residual urine amounting to $1^1/_2$ oz., while the remaining 3 have smaller quantities.

1. See *Lancet*, Feb. 19, p. 312.
2. Lambert, W. *Brit. med. J.* 1945, ii, 403.

Digitized by Google

It appears that a large proportion of cases of mild prostatic obstruction remain mild and that it is misleading to describe this condition as early prostatic obstruction. If all such cases are treated by operation, many unnecessary operations will be performed. It should be our aim rather to develop those operations which can be applied with reasonable safety to the older patients if the condition has shown signs of being progressive.

Glasgow. T. L. CHAPMAN.

THE NICOTINIC-ACID TOLERANCE TEST

SIR,—The work of Professor Véghelyi and Dr. Sass-Kortsák [1] on the nicotinic-acid tolerance test (N.T.T.) originally described by myself seems to justify the claim that the test has practical usefulness as one of many rapid liver-function tests. However, as I pointed out in my original paper [2] and have confirmed in subsequent studies the results of which will be published in due course, certain qualifications must be attached to the interpretation of the N.T.T.

Firstly, it is as reliable or unreliable as any other liver-function test—that is, it can arouse a suspicion but cannot in itself establish a diagnosis. Like all other liver-function tests, it gauges one of the liver's manifold functions—in this case the inflammatory hepatocellular reaction. In chronic cirrhosis or chronic obstructive jaundice the tolerance will be increased only slightly above the maximum "normal" value, which I arbitrarily set at 200 mg.; responses at 300–400 mg. are by no means unusual in these cases.

Secondly, false positive responses are also not uncommon. There is increased tolerance in tuberculosis (300–500 mg.) without other laboratory evidence of hepatocellular damage; this of course does not exclude the existence of such damage. There is also remarkably high tolerance in herpes zoster and similar neurotropic virus infections, with other liver-function tests only showing slight-to-moderate hepatocellular derangement. Thus all that can be said safely is that increased tolerance justifies a careful clinical check-up of the condition of the liver; and, should other evidence of hepatocellular damage be found, changes in tolerance will gauge the progress of the lesion. It is also safe to assume that a normal N.T.T. result excludes the presence of acute hepatitis.

Regarding the influence of food, I cannot confirm Spear's [3] statement that the time of the last meal would grossly influence the test. On the other hand, I have already pointed out that choline and methionine will decrease the tolerance to normal, or nearly normal, values; I have found since the publication of the original paper that a milk diet (5 pints of skimmed milk daily) will also reduce the tolerance, probably owing to its casein content.

Regarding the mechanism of the test, several explanations are possible, though none is yet proved. The evidence—and especially the influence of choline on the tolerance—seems to indicate strongly that the aminisation of nicotinic acid, contrary to Ellinger's [4] suggestion, does take place in the liver, that in hepatitis the body is raided for liver-protecting amino-acids, and that the increased nicotinic-acid tolerance gauges the excess of amino-acids awaiting disposal by that organ. The fact that the liver prefers the aminisation of nicotinic acid to the other method of disposal—namely, conversion to ammonia and urea—opens up the possibility of therapeutic use of nicotinic acid.

I do not know for certain where in the body nicotinic acid is aminised. Dr. Ellinger suspects that it is in the brain. To quote another authority, Dr. C. H. Best,[5] of the Banting Institute, thinks that it is aminised by and in the liver; otherwise the influence of choline on the N.T.T. could not be explained.

I heartily agree with Dr. Véghelyi and Dr. Sass-Kortsák that the N.T.T. at present is simply a clinical observation that probably opens new avenues for further work.

Toronto. A. ERDEI.

1. Véghelyi, P. V., Sass-Kortsák, A. *Lancet*, Jan. 15, p. 126.
2. Erdei, A. *Ibid*, 1948, i, 368.
3. Spear, G. E. *Ibid*, p. 499.
4. Ellinger, P. *Ibid*, p. 539.
5. Personal communication.

Public Health

Influenza

THERE were 259 deaths from influenza in the great towns of England and Wales during the week ended March 5, compared with 251 in the previous week. Sunderland 7 (12) and South Shields 5 (6) had fewer deaths than in the preceding week, but Bradford 11 (3), Leeds 8 (4), and Manchester 23 (16) had increases; deaths in Greater London were about the same, numbering 89 (85). The figures in parentheses are those for the preceding week. In certain places—e.g., Salford and Leeds—incidence has been very high, but the disease has been of a mild type.

Nearly all the isolations of virus have been of the virus A which was prevalent on the Continent, but virus B has been isolated on eggs from material obtained from two outbreaks in public schools.

Yellow Fever in Panama

The Pan-American Sanitary Bureau has been informed of 8 cases of jungle yellow fever, with 6 deaths, at Pacora, some 25 miles from Panama City. These cases, which occurred last November and December, are the first instances of jungle yellow fever in man to be diagnosed in Panama; no clinical case of urban yellow fever has been seen there for fifty years.

The Future of Mass Radiography

There is still no general agreement on how best to use the many new mass-radiography sets which are promised: and a memorandum[1] prepared by the medical members of the council of the National Association for the Prevention of Tuberculosis, under the chairmanship of Dr. R. R. Trail, will provide a useful basis for discussion. The memorandum first expresses fear that control of mass radiography by the tuberculosis committees of the regional boards may prejudice the preventive value of the service; and with a view to minimising this risk, it is proposed that the statistical findings of all investigations should be communicated to the local medical officer of health. Priority, it is suggested, should be given to groups exposed to the risk of developing chronic respiratory disease, including nurses, doctors, and workers in certain dusty occupations; to entrants to all military and civil services; and possibly to such other groups as secondary-school leavers, food-handlers, and expectant mothers. In each area the local health authority should be consulted on the selection of groups; and patients with any symptoms of respiratory disease should go to clinic or hospital. Under present conditions admission to hospital will often not be secured for cases of early pulmonary tuberculosis detected by mass radiography; and chest physicians to whom such patients are referred "should be pressed to give them clinical and radiological review at least every two months." The unit's director should have charge of beds where he can observe some of the doubtful cases, the remainder being referred to the nearest chest clinic. In mass radiography, it is pointed out, the work is often monotonous; and the director's post should be regarded not as a career but as part of the training necessary for a fully qualified physician to a chest clinic. Similarly, radiographers should be engaged for a period of service with units under the terms of appointment to chest clinics.

The council contends that, with the comparatively few sets now in operation, it is better to concentrate on serial examination of those specially vulnerable than to take groups at random and make no further re-examination for one or two years. With the introduction of B.C.G. vaccination, the calls on the mass-radiography service are likely to increase; and wherever possible, tuberculin skin-testing should be performed when the miniature radiograph is taken. Two possible lines of research are: (*a*) serial radiography and tuberculin testing of closed communities; and (*b*) a follow-up of normal school-leavers over a period of some ten years.

1. *Med. Offr*, March 12, p. 116.

Digitized by Google

Public enthusiasm for mass radiography, the memorandum concludes, seems to be waning; and the association is turning its attention to the production of explanatory leaflets and pamphlets and of posters; it is also considering how best a suitable, realistic film can be made. There is need for lectures and talks, particularly by young people.

Parliament

QUESTION TIME

Fat-content of Ice-cream

Mr. C. W. DUMPLETON asked the Minister of Food what conditions as to the fat-content of ice-cream were made when allocations of sugar were made to the manufacturers.—Dr. EDITH SUMMERSKILL: No such conditions are attached to normal allocations of sugar; but an extra allowance of 15% is granted to manufacturers who undertake to maintain a minimum fat-content of 2½%.

Mr. SOMERVILLE HASTINGS: Does the Minister realise what dreadful stuff is now being sold as ice-cream and how small is the fat-content in a great deal of it?—Dr. SUMMERSKILL: I would like to prescribe a standard, but the shortage of milk and milk powder makes it impossible for us to prescribe a satisfactory product, and that is why we have hestitated to do it.

Tuberculosis in the Navy

On March 8 in the House of Commons Mr. JOHN DUGDALE, parliamentary and financial secretary to the Admiralty, in introducing the Navy Estimates for 1949–50 and Navy Supplementary Estimate for 1948–49, said that during the past year 19,700 men had been accepted for the Royal Navy, which was very nearly the Admiralty's target for recruitment. There was one difficulty today which he thought was greater than before the war, and that was the high proportion of wastage. For example, before the war 2 men per 1000 were invalided for tuberculosis. Today they were invalided at the rate of 7 per 1000. This was not due to an increase of tuberculosis in the Navy, but to the fact that there was now a system of examination which enabled the disease to be detected at a much earlier stage.

Patients' Travelling Expenses

Mr. GORONWY ROBERTS asked the Minister of Health why hospital management committees were applying a means test to patients before reimbursing them in respect of travelling expenses between home and hospital.—Mr. A. BEVAN replied: Expenses are payable only in case of hardship, but no means test should be applied. The main test should be the length of journey.

Cremation Certificates

Mrs. C. S. GANLEY asked the Minister whether he would consider fixing a standard fee for doctors and hospitals signing cremation certificates.—Mr. BEVAN replied: I have no authority to fix a standard fee for cremation certificates.

Remuneration for Temporary Residents

Colonel M. STODDART-SCOTT asked the Minister whether it had yet been decided upon what principles doctors in the National Health Service were to be paid for the treatment of temporary residents, visitors, holidaymakers, foreigners, and those patients not on the doctor's list; and how much money was available for this service.—Mr. BEVAN replied: I am still discussing with the profession the principles on which such payments will be made in future. The total amount of these payments depends on the number of persons involved and is a charge on the central pool for the remuneration of general medical practitioners. I have agreed with the profession that payment in respect of the period July 5 to Dec. 31, 1948, shall broadly be on the same basis as under the National Health Insurance arrangements.

In answer to a further question he added that payments for this period would be made on March 31, 1949. These payments were necessarily made in arrear and payment for the period Jan. 1 to March 31, 1949, would be made on June 30, 1949.

Obituary

GEORGE COCKCROFT

M.B. LOND.

THE death of Dr. Cockcroft, of Middleham, on Feb. 24, marks what may be called the end of a dynasty; for he was the last of a line of doctors of his own kin, reaching back to 1780, who practised in this North Riding town.

As a neighbour and friend for over 35 years, I feel qualified to write this notice about him, and, as one privileged to listen to his lecture on 200 Years of Country Practice, to write something about this remarkable practice, only the first holder of which was of different extraction. Those of us who were present at this lecture sat enthralled while he described the sequence of these rugged individualists and while he gave extracts from his own poems; and he was a poet of no mean stature. He traced the sequence of only five principals, describing their dress, how they travelled the rough roads, and what remedies they employed (all culled from extant practice records), what they charged for their services, and the detailed accounts they rendered to their patients—the very instruments, still in his possession, which they used. It was an epic deserving wider publication, which his modesty forbade.

George Cockcroft, the son of William Cockcroft, solicitor, was born at Rochdale in 1882. He was the grandson of Dr. William Cockcroft, of Middleham. Educated at Rossall, he went up the school in phenomenally brief time to become head boy and gain a scholarship to Guy's Hospital. His hospital career was brilliant, including the award at Guy's of the Treasurer's gold medal in clinical surgery, the medal and exhibition in anatomy, and the University of London medal in medicine and surgery. Everything pointed to a successful consultant career; but, with a philosophy which was already his, he decided to go back to the family practice in Middleham, the Newmarket of the North, at the foot of beautiful Wensleydale. That decision has for more than 40 years meant much to Lower Wensleydale. His reward is in the hearts of his patients; and those of us, 550 in all, who attended the memorial service in St. Mary and St. Alkelda's Church in Middleham, where Charles Kingsley was the last of the canons of the collegiate church, were deeply moved by the obvious place he had in the affections of those whom he had served so long and faithfully.

To spend an hour with him was a memorable experience. Subconsciously one would find how deeply versed he was in classical lore, in history (especially that connected with his beloved dale and his beloved castle), and in the science and art of medicine. And then he had such a sense of fun. His tales of his years of practice showed this clearly, and with it his kindly attitude towards his patients. He was intensely interested in and truly loved human beings, and this is what made "Dr. George" the hero of Middleham for more than a generation.

As a neighbouring colleague, I am in a position to judge his great professional ability. In country practice we still call upon our neighbours in consultation, and never was my confidence in him misplaced. He was one of those doctors of whom it can be truly said that he put the welfare of his patients far beyond his own professional reputation. He wrote little to the medical press, but his friends rejoiced that of late years he had so foregone his modesty as to lecture to medical students and medical societies. His life has been cut short at a point when his influence would have been great in bringing tradition to the rising generation. Also he was the only outstanding authority on the history of Wensleydale, particularly of Middleham Castle, and his local

Digitized by Google

audiences had the benefit of this, almost to the day of his death.

In the first world war he served in a London field ambulance in Palestine, and was one of the first to enter Jerusalem.

One must not forget his great work as M.O.H., his striving to bring pure water and decent housing to those for whom he was responsible for 42 years, and his especial concern for the care of the aged. His sturdy figure, his abundant white hair, and his singularly charming smile and hearty laugh, will remain long in the memory of those who knew him. It is probable he realised he had not long to live. He once said to me: "A stroke is a grand thing so long as it does its job properly." He worked until an hour before the stroke which rendered him unconscious and brought his life to a close.—This was one of his verses:

> "What do you see at end of the road,
> That you strain so, Son of mine?
> Only the place, where we drop the load,
> Fate piled on us, Mother o'mine."

In 1914, he married Mary, daughter of the late Matthew Dobson Peacock, the well-known trainer, and she survives him.

W. N. P.

ETHEL VAUGHAN-SAWYER

M.D. LOND.

Dr. Vaughan-Sawyer, consulting gynæcologist to the Royal Free Hospital, who died at Mount Vernon Hospital on March 9, was born in 1868, the daughter of Cedric Vaughan, J.P., of Millom, Cumberland. After early education at Lausanne and University College, London, she was in 1891 enrolled as the 333rd student of the London School of Medicine for Women. During her undergraduate course she won many prizes and she graduated M.B. with honours in 1896, taking the M.D. two years later. After working at Camberwell Infirmary as assistant medical officer in 1899, she was appointed pathologist to the Royal Free Hospital, and in 1902 assistant physician for diseases of women and assistant obstetrician to the hospital and lecturer in gynæcology in the University of London. On the retirement of Mrs. Scharlieb in 1908 Miss Vaughan became senior gynæcologist and obstetrician. A severe attack of glaucoma compelled her to retire from the hospital and from active surgery in 1928, and despite remissions, her eyesight gradually failed; for the last ten years of her life she was completely blind. She taught herself Braille and continued to live in her house in Harley Street until the last couple of years which were spent in a home where she was happy and received every care.

G. M. S., to whom we owe this memoir, writes: "Many generations of students of the Royal Free Hospital School of Medicine remember Mrs. Vaughan-Sawyer with immense gratitude for her teaching. She was a vivid personality, an excellent diagnostician, and a meticulously careful surgeon. Particularly successful in the performance of Wertheim's hysterectomy for cancer of the ceryix uteri, she used to operate on women whose disease was more advanced than would have been attempted by most surgeons at that time. In those days follow-up clinics for cancer patients were rare, but her cases were seen at regular intervals, and when the disease had recurred she used to send parcels of food and fruit and flowers to her poor women, living mostly in tenements around King's Cross and the Caledonian Road. But her kindness and generosity were unbounded, both to her patients and to her old students and residents.

"Her great success both in hospital and private practice was due to her superb surgical skill, and to the great interest she took in the lives of her patients. This interest remained with her even after her retirement, and she dearly loved a gossip about the doings of her old students and about the affairs of her old medical school and hospital. 'Tottie,' as she was affectionately called, was an essentially human woman. She loved the pleasures of life—good food, good wine, an evening playing bridge—and though often casually, and always unfashionably, dressed she delighted in seeing people smartly and expensively attired. She was a most entertaining conversationalist, with a characteristic chuckle, and her fund of stories, though often unsuited to a drawing-room, never failed to drive home a point to a class of students. It is doubtful whether, at the time, the student always realised how good was her chief's teaching; but once she had started in practice, it was surprising how often she found Mrs. Vaughan-Sawyer had impressed upon her just the facts that were really needed in dealing with women patients. Despite all her family griefs and her progressive ill health, Dr. Vaughan-Sawyer still managed to enjoy the company of her friends, and they were legion. Even within two weeks of her death she was able to say with almost her old sparkle: 'You know, I've had a wonderful life, and am still thrilled when I think about it.' It is this aspect of her personality that will live longest in the memory of those who admired her gallantry so much."

On her marriage to Captain Henry Sawyer, Indian Army, she took the name of Vaughan-Sawyer. Her married life was extremely happy and she never ceased to mourn her husband's death in action in 1914. There was one daughter of the marriage who died in girlhood.

Diary of the Week

MARCH 20 TO 26

Monday, 21st

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. F. S. Gorrill: Anatomy and Physiology of Bone—Part II. (Arnott demonstration.)

HUNTERIAN SOCIETY
7.30 P.M. (Talbot Restaurant, 64, London Wall, E.C.2.) Dr. William Evans, Dr. Geoffrey Bourne, Mr. George Mason: Treatment of Coronary Thrombosis.

Tuesday, 22nd

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. W. E. Gye, F.R.S.: Propagation of Mouse Tumours by Means of Dried Tissue. (Imperial Cancer Research Fund lecture.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Mr. A. K. Monro: Varicose Conditions of the Lower Limb.

CHADWICK LECTURE
4.30 P.M. (Westminster Medical School, Horseferry Road, S.W.1.) Dr. Helen Mackay: A Health Service for Children.

ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. Dr. Ronald MacKeith: Visual Aids in Pædiatrics.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Mr. J. C. Trevor: Some Problems of Race.

Wednesday, 23rd

ROYAL COLLEGE OF SURGEONS
5 P.M. Dr. Frank E. Adair (New York): Results of Surgery in the Treatment of Breast Cancer. (Moynihan lecture.)

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Mr. L. Z. Cosin: Social Significance of Geriatric Rehabilitation.

MEDICO-LEGAL SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Miss Rebecca West: Lynching Trials in America.

SOCIETY OF CHEMICAL INDUSTRY
6.15 P.M. *Nutrition Panel* (Gas Industry House, Grosvenor Place, S.W.1). Prof. John Beattie: Effect of Non-protein Calories on the Utilisation of Proteins.

Thursday, 24th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. Kenneth Bowes: Infra-red Photographic Studies of the Superficial Veins in the Female. (Arris and Gale lecture.)

Friday, 25th

ROYAL COLLEGE OF SURGEONS
5 P.M. Dr. W. S. C. Copeman: Pathological Anatomy of Certain Forms of Lumbar Fibrositis and the Rôle of Surgery in its Treatment. (Hunterian lecture.)

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, W.1
8 P.M. Dr. David Nabarro: Congenital Syphilis.

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Dr. H. V. Morlock: Indications for Bronchoscopy in Chest Diseases.

BIOCHEMICAL SOCIETY
11 A.M. (University College, Gower Street, W.C.1.) Short papers.

ROYAL COLLEGE OF PHYSICIANS, 9, Queen Street, Edinburgh
5 P.M. Dr. Ian Hill: Multiple Head Electrocardiograms. (Alexander Gibson lecture.)

Saturday, 26th

ST. STEPHEN'S HOSPITAL, Fulham Road, S.W.10
10 A.M. Prof. Bruce Perry: Ætiology of Acute Rheumatism. (Introductory address to a weekend course.)

Digitized by Google

Notes and News

APPEAL TRIBUNAL

THE membership has now been announced of the tribunal established under the National Health Service Act, 1946, to inquire "into cases where representations are made that the continued inclusion of a person on the list of an executive council would be prejudicial to the efficiency of the service in which that person is participating." The Lord Chancellor has appointed Sir Reginald Sharpe, K.C., to be the chairman of the tribunal. The Minister of Health, after consultation with the associations of executive councils, has appointed Mr. Henry Lesser, O.B.E., LL.B., to be a member of the tribunal. The third member will be selected, according to the profession of the person whose case is being investigated, from the following panel which has been appointed by the Minister after consultations with the organisations representative of the professions concerned: Dr. S. A. Winstanley (medical practitioner), Mr. L. C. Attkins, F.D.S. R.C.S. (dental practitioner), Mr. G. H. M. Graham, M.P.S. (registered pharmacist), Dr. E. G. Mackie (ophthalmic medical practitioner), Mr. W. B. Barker, F.B.O.A. (ophthalmic optician), Mr. J. R. Howard, F.A.D.O. (dispensing optician). The clerk to the tribunal, appointed by the chairman with the Minister's approval, is Mr. R. B. Cooke, solicitor, 5, Verulam Buildings, Gray's Inn, London, W.C.1.

CAMBRIDGE EXAMINATIONS

WITH the help of an advisory committee of Cambridge graduates who hold clinical teaching appointments in the London medical schools and who have been examiners for the final M.B. examination, the faculty board of medicine have considered the recommendations made by the General Medical Council in 1947 on the revision of the curriculum and examinations. The board propose that there should be a rearrangement of the subjects of the two parts of the final M.B. examination. Pathology, pharmacology, and therapeutics are basic subjects necessary for a proper understanding of medicine, surgery, and midwifery and gynæcology, and the board think that as such they should form the subjects of the first part and should be taken after $2^1/_2$ years' clinical study. They consider that the three main clinical subjects (medicine, surgery, and midwifery and gynæcology) should be taken together after 3 years' clinical study and form the second part of the final M.B. examination. They also consider that at the first attempt a candidate should have no option but to take these three main clinical subjects simultaneously, but that a pass should be permitted in one or more subjects provided that a reasonable standard is attained in the remaining subject or subjects. The board also propose that in the first part the scope and character of the examinations in pathology and pharmacology should be the same as for the present examinations in those subjects. Pathology should include bacteriology, preventive medicine from the aspect of communicable diseases, and the pathological aspects of forensic medicine. Pharmacology (including therapeutics and toxicology) should avoid undue emphasis on the academic side of pharmacology and there should be no practical examination. The general form of the separate subjects of the second part should be much the same as the present form of examination in those subjects, but papers in medicine should cover the ancillary subjects—pædiatrics, social medicine, and psychiatry.

INDIAN MEDICAL RESEARCH

THE annual report for 1947 of the Scientific Advisory Board, issued by the governing body of the Indian Research Fund Association, records another year of satisfactory progress. In trials of various preparations of D.D.T. as indoor residual sprays against adult mosquitoes, it was found that a stirrup-pump fitted with a suitable nozzle proved simpler, and answered the purpose better, than other types of equipment. Field trials were conducted, under the ægis of the Calcutta School of Tropical Medicine, to test the action of sulphaguanidine against cholera; this drug acts best during the early stages of the disease. Therapeutic trials with sulphaguanidine, sulphadiazine, and phthalysulphathiazole, conducted under hospital conditions in Calcutta, indicated that sulphaguanidine is the most effective. Three drugs of the sulphone group—'Promin,' 'Diasone,' and 'Sulphetrone'—were tested in the treatment of leprosy at the Tropical School of Medicine, Calcutta, with encouraging results. Although found to have certain limitations, they proved particularly valuable where injections of hydnocarpus oil are not tolerated. Field trials of sulphadiazine and sulphamerazine in bubonic plague were carried out under the direction of the director of the Haffkine Institute, Bombay. Sulphamerazine appears to be the drug of choice, because it gives the desired concentration in the blood with smaller doses administered at less frequent intervals. Streptomycin was tested in experimental plague in animals, with striking results; and its use is being extended to the treatment of plague in man.

The nutritive value of soya-bean milk and soya-bean curd are being examined at the Indian Institute of Science, Bangalore. These are palatable and nutritious, and experimental feeding trials indicate that soya-bean milk and products can provide a reasonably cheap and satisfactory substitute for cow's milk. The government of India have decided to set up a factory in Bombay for manufacturing penicillin and sulpha and antimalarial drugs. Production is scheduled to start in three years' time.

CENTENARY AT WATFORD

ON March 11, 1849, the West Herts Medical Society was formed by a group of seven doctors who met at the Rose and Crown Hotel, Watford. For many years the society was essentially a dining club, but gradually medical topics took pride of place. The town of Watford having grown in size and importance, a separate society was founded there in 1896, but in 1912 this was fused with the senior society.

Dr. C. Herbert Hall, a founder member of the Watford society, and for the past 53 years secretary of this and later of the combined body, was among those who last week attended a dinner held in Watford to celebrate the centenary. Dr. F. M. R. Walshe, F.R.S., spoke of the value of such a body in arousing a sense of continuity with the past, and in promoting mutual regard and respect. Local societies, he observed, become the focus of loyalties which larger associations do not command; and their continuance is vital to the survival of medicine as a humane profession. In his reply, Dr. J. W. C. Leech, the president, referred to the influence of the Watford society in sustaining a feeling of friendship among the doctors of the neighbourhood. Lord Moran, F.R.C.P., and Sir William Gilliatt, F.R.C.O.G., responded to the toast of The Guests, proposed by Dr. F. J. Aldridge.

A G.P. LOOKS BACK

A DOCTOR who can review sixty years of medical life has seen his profession shoot up and branch like the mango tree in the Indian trick. Dr. H. W. Pooler qualified in Birmingham in the days when Jordan Lloyd, his chief, could look up from an amputation to the young man loitering in the theatre in a lounge suit, and say "Now, Mr. Pooler, take your hands out of your pockets and come and hold this leg." In his autobiography,[1] Dr. Pooler sketches pleasantly, if superficially, the great revolution of thought and practice in which he has participated. It is a placid chronicle of steady work and some considerable achievements, starred with agreeable anecdotes and informed throughout by what he describes as his "inveterate optimism"—though it might more fairly be called his confidence that the universe somehow makes sense. When a man who has had more than eighty years of it believes this, the rest of us should not feel disheartened: Dr. Pooler's book is a tonic, elegantly and blandly presented.

University of Oxford

The University Grants Committee have given £193,500 towards the cost of the erection of a physiology laboratory.

Ophthalmological Society of the United Kingdom

The annual congress of the society is to be held at 1, Wimpole Street, London, W.1, on Thursday, Friday, and Saturday, March 31, April 1, and 2, under the presidency of Mr. F. A. Juler, who will give an address on the Operation for Acute Glaucoma and on Refraction. The programme also includes a discussion on corneal grafting when the opening speakers will be Prof. A. Franceschetti, Mr. J. W. Tudor Thomas, Prof. G. P. Sourdille, Mr. B. W. Rycroft, and Mr. D. P. Choyce.

1. My Life in General Practice. London: Christopher Johnson. 1948. Pp. 194. 15s.

Digitized by Google

Royal College of Surgeons of England

At a meeting of the council held on March 10, with Lord Webb-Johnson, the president, in the chair, Hunterian professorships were awarded to Prof. C. F. M. Saint of South Africa and Prof. Robert Harris of Toronto. Prof. W. E. Gye, F.R.S., was elected an emeritus professor of the college from the date of his retirement from the directorship of the Imperial Cancer Research Fund.

A Leverhulme scholarship was awarded to Mr. W. J. Dempster of the Postgraduate Medical School of London. Diplomas in public health were granted jointly with the Royal College of Physicians to P. L. Karney and D. F. van Zwanenberg.

Royal Appointment

Dr. J. L. B. Ansell has been appointed surgeon apothecary to the Royal Household at Sandringham in succession to the late Sir Frederic Willans.

Auxiliary Royal Army Medical Funds

The annual general meeting of members will be held at 11, Chandos Street, London, W.1, on Monday, April 4, at 5.30 P.M.

Royal Microscopical Society

On Wednesday, April 6, at 5 P.M., at B.M.A. House, Tavistock Square, London, W.C.1, Dr. J. A. Murray, F.R.S., will be admitted to the honorary fellowship of the society.

British Schools Exploring Society

Applications are invited for the post of an honorary surgeon for the Northern Norway expedition, leaving on Aug. 3 and returning on Sept. 20. Further particulars will be found in our advertisement columns.

CMF/MEF Physicians

A reunion dinner will be held on Saturday, April 2, at Simpson's in the Strand, with Dr. E. R. Cullinan in the chair. Further particulars may be had from Dr. Arthur Willcox, hon. secretary, 66, Harley Street, W.1.

Alexander Pigott Wernher Memorial Trust

The trustees have lately allocated £60,000 for the use of the Medical Research Council in accordance with the objects of the fund, which are "the prevention and cure of blindness and deafness in the United Kingdom and British Empire, and in particular research in connexion therewith by financing medical men and students within the Empire to study methods and practices in all countries of the world." The fund will ultimately reach about £300,000.

Chair of Pædiatrics for Wales

The council of the Welsh National School of Medicine is submitting to the University Grants Committee a proposal to set up a chair of pædiatrics and child health at Cardiff. The department will be in the charge of a whole-time professor with two senior assistants. Subject to the approval of the governors of the United Cardiff Hospitals 80 beds will be provided at Llandough Hospital and 17 at Cardiff Royal Infirmary. Instruction on the newborn will remain at the obstetric centres at the infirmary and St. David's Hospital.

Residential Club for Hospital Staff

The board of governors of Middlesex Hospital are buying, with part of their endowment capital, the Marlborough Court Hotel, Lancaster Gate, to use as a residential club for some of their staff and students. The charge for the rooms will cover running expenses, and no cost will therefore fall on public funds. Accommodation is planned for 160 people, including medical officers of registrar status, almoners, physiotherapists, radiographers, members of the administrative staff, and women students of the medical and ancillary schools. There will also be room for a few married medical students.

Health Congress at Brighton

At the preventive medicine section of the congress which the Royal Sanitary Institute is holding in Brighton from May 23 to 27, Brigadier H. L. Glyn Hughes will open a discussion on the Hospital and Medical Services. At the conference of medical officers of health Dr. C. Metcalfe Brown will speak on Public Health Research, and Dr. J. Stevenson Logan will introduce a debate For and Against Institutional Midwifery. In the tropical hygiene section Dr. P. C. C. Garnham will read a paper on Modern Concepts in Malaria Control, and Dr. W. Berry on the West African Groundnut Scheme.

Medical Society for the Care of the Elderly

A meeting of this society will be held on April 1 and 2 at Belmont Road Hospital, Liverpool, when Lord Amulree, Dr. J. W. Affleck, and Dr. Marjory Warren will be among the speakers. Further particulars may be had from Dr. Trevor Howell, hon. secretary, St. John's Hospital, St. John's Hill, London, S.W.11.

British Medical Association in Australia

Mr. Victor Hurley, president of the Royal Melbourne Hospital, has been appointed federal president of the B.M.A. in place of Sir Henry Newland, who has resigned after holding office for 20 years.

Mr. Hurley was director-general of medical services in the Royal Australian Air Force during the war. He is a vice-president of the Royal Australasian College of Surgeons.

Scottish Conjoint Board

On March 8 the following, having passed the final examination, were admitted licentiates of the Royal Colleges of Physicians and Surgeons of Edinburgh, and the Royal Faculty of Physicians and Surgeons of Glasgow:

Abd-El-Rahman Azzam, Elspeth V. Beveridge, Mahala M. Beveridge, Andre Carlos, Elizabeth Carwardine, J. C. Cassaglia, S. H. Curry, S. B. Davies, I. M. Downie, K. A. H. Fermie, W. O'C. FitzPatrick, R. M. Gaze, James Govan, J. G. Hart, Mary M. Hay, Lysbeth R. Hurwich, Margaret J. G. Jamieson, J. H. Kennedy, J. J. O'B. Lavery, James Leonard, D. W. Lyon, G. J. McCann, Sushil Mallick, J. C. Marshall, H. P. P. Morris, J. S. Nelson, Joseph Ryan, Samuel Schlifka, J. G. Sheehy, Isidore Tandatnick, Francis Whyte, H. N. R. Wilson, N. W. Wilson, Matthew Wotherspoon, J. C. Wright.

Health Services in Northern Ireland

Speaking in the Northern Ireland House of Commons last week, Captain T. O'Neill, the parliamentary secretary to the ministry of health and local government, said that by January of this year there had been 175,000 applications for dental treatment, and in over 100,000 cases treatment had been completed. While there were grounds for satisfaction here, he added that the considerable outlay in payments to dentists was a matter of concern. Applications continued at a high level. The number of prescriptions dispensed by chemists in January totalled over 370,000 and cost £90,000. If maintained at that level, payments for prescriptions in a full year would exceed £1 million. By Dec. 1, 120,000 persons had had their sight tested. The cost of the supplementary eye services was expected to be £285,000 greater than was estimated.

Medical Society of London

Presiding over the 169th anniversary dinner on March 8, Dr. T. Jenner Hoskin recalled some of the vicissitudes through which the society had passed since its foundation in 1773. In 1805 what was now the Royal Society of Medicine was founded by dissident members, largely because their president had held his position for 22 years. At first the members were 30 physicians, 30 surgeons, and 30 apothecaries, and the president was always a physician; but for more than a century the physicians and surgeons had alternated in the chair. In its fourth home, in Chandos Street, occupied since 1871, the society was now flourishing, with assets around £30,000. Meetings were very well attended, and, as Lettsom the founder desired, they gave practitioners frequent opportunities of congregating to discuss interesting cases or to communicate discoveries made at home or abroad. Mr. Bernard Darwin, the principal guest, felt that it was a work of supererogation for a layman to propose the health of a medical society, and spoke of the serenity he had gained through having to give up golf. The golfing temperament was not what it was in the days when a player said to his erring putter "you little brute, don't presume on my good nature any longer" and beat it to pieces on a wall; or when another laid all his clubs carefully on the rails in front of an approaching train. The golfer had a niggardly habit of trying to cure his diseases without professional advice; "and on the whole I believe he's right." However, professionals were now giving lessons to groups of youngsters simply for the good of the game, which seemed to be the beginning of a free Golfing Medical Service. Mr. E. W. Riches, proposing The Visitors, recalled that Mr. Darwin's forebear, Erasmus Darwin, was a physician at Lichfield; but legend said that he was paid a guinea a line for his verse, which he probably preferred to a guinea a mile for his visits. Lord Moran, in praising Mr. Darwin as golfer and writer, remarked that happiness consists in finding out what you want to do and doing it all the time—preferably in the open air. He related some of his own experiences "before I made the discovery that I was a natural non-golfer."

Digitized by Google

World Health Organisation

The executive board has accepted the following draft programme and budget of W.H.O. for 1950:

(1) The regular budget, totalling $8,150,110, comprising administrative expenses and an operating programme to be financed by contributions from all members according to the constitution.

(2) A supplemental operating programme of advisory and technical services in the amount of $13,619,180. Governments would be invited to come to the second World Health Assembly prepared to make additional contributions to W.H.O. in order to finance this programme on a basis to be determined by negotiations.

The programme will be submitted to the second World Health Assembly which meets in Rome on June 13.

The Working Party, who drew up the programme, had decided by 4 votes to 3 against budgeting for supplies to governments. In supporting this principle Dr. K. Evang (Norway) pointed out that supplies in the amount of $2 million would be allotted to the demonstration teams initiating public-health programmes. It was also unanimously agreed that W.H.O. would supply governments in emergencies. Moreover, W.H.O. had already created a medical supply bureau to advise governments on how to procure medical and public-health equipment. The question was whether W.H.O. should become truly a supply agency. The Working Party, Dr. Evang concluded, had decided that this was not an essential function of the organisation, and believed that the obtaining of these commodities was basically an economic problem. Dr. Melville Mackenzie (U.K.) while recognising the critical need for health and medical supplies in many areas of the world, felt that W.H.O. should use its influence to assist governments in utilising existing international economic machinery to obtain supplies. He warned that a chaotic situation might ensue if W.H.O. undertook procurement and distribution of health supplies in addition to its other functions. On the other hand Dr. A. Stampar (Yugoslavia) declared that a state of emergency existed now and would continue for several years in many countries, especially in Europe. Unless W.H.O. recognised this fact and acted accordingly, it might mean the end of the organisation.

After further discussion it was decided, by a vote of 14 to 1, that W.H.O. would provide medical supplies to governments. The text of the decision was as follows:

The board is of opinion that it is not within the province of W.H.O. nor is it possible for the organisation to make itself responsible for supplies to different countries. But the board recognises that it may be desirable in some cases for supplies to be made available for specific projects examined in advance in detail and approved by the executive board, either to continue the implementation of programmes after the W.H.O. demonstration teams have finished their task, or to implement or further a health project to be carried out by a governmental health administration. Governments will pay for these supplies wherever possible

The budget for 1950 makes provision for the following projects: mental health ($942,550), environmental sanitation ($1,090,290), tuberculosis ($632,720), venereal diseases ($791,135), mother and child health ($1,114,040), cholera ($177,215), nutrition ($408,285), public-health administration ($488,690), typhus ($181,315), and plague ($209,965).

The mental-health programme, which is the first international plan of its kind, has been prepared according to recommendations made by the World Federation of Mental Health. It includes the collection and dissemination of information, field surveys in rural communities, in industrial units, and among students, and 6 travelling seminar teams to demonstrate methods of survey, prevention, and treatment of mental disorder.

The appropriation for the tuberculosis research programme to evaluate the effectiveness of B.C.G. vaccination has been increased from $100,000 to $300,000. The board has also recommended the convening of an international conference on immunisation procedures as soon as possible, to bring together epidemiologists, pædiatricians, and vaccine experts to discuss the use of new techniques for producing more effective vaccines and to elaborate plans for the widespread application of immunisation.

The board decided unanimously that a regional organisation for Europe should be established in the near future, as soon as the majority of governments concerned agree upon it. It will be recalled that a special office for war-devastated countries in Europe was set up in Geneva on Jan. 1, 1949.

Ecuador has joined W.H.O., bringing the number of member nations to 59.

Prof. G. Grey Turner has been elected an hon. foreign member of the Société de Chirurgie de Lyon.

Appointments

ANDERSON, D. E. W., M.R.C.S., D.P.M.: deputy medical superintendent, Royal Earlswood Institution, Redhill, Surrey.
ARONSON, R. P., M.B. Lond., M.R.C.P.: pædiatric registrar, Nottingham Children's Hospital and Nottingham City General Hospital.
BRAMLEY, G. F., M.D. Leeds, D.P.H.: county M.O. and school M.O. Gloucestershire.
BRYAN, H. S., M.R.C.S.: medical director, central child psychiatric clinic, Alder Hey Hospital, Liverpool.
CAMPBELL, I. D., M.B. Edin.: M.O., Leeds Regional Hospital Board.
CRANNA, D. D., M.B. Manc., F.R.C.S.: asst. orthopædic surgeon, Salford Hospital Centre.
MIDDLEMISS, J. H., M.D. Durh., D.M.R.D., F.F.R.: director of radiodiagnostic department, United Bristol Hospitals.
PIRRIE, G. D., B.A., M.B. Camb., D.P.H.: a senior M.O., public-health department, London County Council.

University College Hospital, London:

AMULREE, Lord, M.A., M.D. Camb., F.R.C.P.: asst. general physician i.c. chronic sick wards at St. Pancras Hospital.
MERRINGTON, W. R., M.S., B.SC. Lond., F.R.C.S.; asst. general surgeon.
WOLFE, H. R. I., M.S. Lond., F.R.C.S.: asst. general surgeon.

Hospital for Sick Children, Great Ormond Street, London:

ARNOTT, D. C., M.B. Lond., D.C.H.: registrar, department of physical medicine.
ARTHURTON, M. W., M.B. Lond., D.C.H.: house-physician.
BLAXLAND, P. J., M.B. Lond., F.R.C.S.: surgical registrar.
CHAMPION, E. P., M.B.: junior anæsthetics registrar.
CRAWSHAW, E. G. A., M.B. Camb., M.R.C.P., D.C.H.: asst. medical registrar.
DAWSON, R. L. G., F.R.C.S.: part-time surgical registrar.
FATHI, J. T., M.S. Lond., F.R.C.S.: part-time surgical registrar.
HOPE, E. V., B.A., M.B. Camb., F.R.C.S.: part-time surgical registrar.
JOLLY, H. R., M.A., M.B. Camb., M.R.C.P.: asst. medical registrar.
LOVEL, K. W., M.A., B.M. Oxfd: asst. medical registrar.
MACKENZIE, ALICE, M.D. Aberd.: asst. medical registrar.
MACLEAN, W. E., M.D. St. And., M.R.C.P., D.C.H.: asst. medical registrar.
MACOUN, S. J. R., B.A., M.B. Camb., M.R.C.P.: asst. medical registrar.
MANN, T. P., M.D. Lond., M.R.C.P., D.C.H.: asst. medical registrar.
NIXON, H. H., M.A., M.B. Camb., F.R.C.S.: surgical registrar.
PERCIVAL, R. H., M.A., B.M. Oxfd, F.R.C.S.: surgical registrar.
PUGH, J. P., M.B. Birm., M.R.C.P., D.C.H.: asst. medical registrar.
SAVAGE, T. R., M.A., B.M. Oxfd, M.R.C.P.: asst. medical registrar.
STANFIELD, MARGARET, M.B. Lond., D.C.H.: asst. medical registrar.
VULLIAMY, D. G., B.A., M.B. Camb., D.C.H.: asst. medical registrar.
WILLIAMS, D. I., M.A., M.CHIR. Camb., F.R.C.S.: part-time surgical registrar.

Births, Marriages, and Deaths

BIRTHS

ARONSON.—On March 7, in London, the wife of Dr. R. P. Aronson—a daughter.
BARCLAY.—On March 7, at Middlesbrough, the wife of Dr. P. M. Barclay—a son.
BURGE.—On March 3, in London, the wife of Mr. Harold Burge, M.B.E., F.R.C.S.—a son.
CHETWYND.—On Feb. 28, the wife of Dr. J. B. Chetwynd—a son.
CONDON.—On March 8, the wife of Dr. H. A. Condon—a daughter.
JORDAN.—On March 4, at Sheffield, the wife of Dr. Arthur Jordan—a daughter.
MANNING.—On Feb. 20, in Belfast, the wife of Dr. F. E. B. Manning—a son.
MARSHALL.—On March 6, at Banstead, Surrey, the wife of Dr. J. K. Marshall—a son.
PORTCH.—On March 1, at Caythorpe, the wife of Dr. G. G. Portch—a son.
STANNING.—On Feb. 16, at Milford-on-Sea, Hants, to Dr. Kathleen Stanning (née Gillett), wife of Mr. John Stanning—a son.
TAYLOR.—On Feb. 17, in London, to Dr. Jill Taylor (née Weatherill), wife of Mr. R. W. Taylor—a son.
THOMAS.—On March 7, the wife of Dr. Merley Thomas—a son.
THURLOW.—On March 3, at Axminster, the wife of Dr. G. W. Thurlow—a daughter.
WHARTON.—On March 5, at Colwyn Bay, the wife of Dr. D. O. Wharton—a daughter.
WILLCOX.—On March 5, at Leamington Spa, the wife of Dr. J. M. Willcox, M.C.—a daughter.

DEATHS

BUCK.—On March 9, Arthur Herbert Buck, F.R.C.S., aged 79.
FRENCH.—On March 5, at Burgh Heath, Ronald Edgar French, M.A., M.D. Camb.
HAY.—On March 9, Alexander Robertson Forrest Hay, M.B. Glasg., aged 66.
HAYWARD.—On March 12, at Wilton, Wilts, John Arthur Hayward, M.D. Lond., F.R.C.S., M.R.C.P., aged 83.
MARTIN.—On March 12, Alfred Eugene Martin, M.A., M.D. Camb., aged 74.
MEADE.—On March 5, at Harrogate, Warren Meade, M.R.C.S., aged 74.
VAUGHAN-SAWYER.—On March 9, at Northwood, Ethel May Vaughan-Sawyer, M.D. Lond.
WEST.—On March 6, at Fleet, Hants, John Weir West, C.B., C.M.G., C.B.E., major-general, A.M.S. retd.
WYNNE.—On March 7, at Northiam, Sussex, Walter Wynne, M.B. Edin., aged 81.

Digitized by Google

HISTORICAL BUILDING
DES MOINES, IOWA

AT THE CROSS-ROADS

THE DEVELOPMENT OF OUR HEALTH SERVICES*

A. LESLIE BANKS
M.A. Camb., M.D. Lond., F.R.C.P., D.P.H.
A PRINCIPAL MEDICAL OFFICER OF THE MINISTRY OF HEALTH

THERE are two periods in English history which at first sight appear to be completely divorced from each other but which to students of social welfare present not only interesting contrasts but a thread of unity.

In A.D. 597 Augustine introduced Christianity to England, and from that time until the dissolution of the monasteries by Henry VIII in 1535–37, the principles of medieval Christianity held sway. From the health point of view the faults were many. The contempt for personal cleanliness, the dis-regard, indeed dis-esteem in which family life was held, combined with a degree of credulity amounting to unquestioning belief in the supernatural, tended to produce a state of mind in which scientific inquiry could not exist. Application of the principles of hygiene, and indeed any rational procedures in medicine, were therefore impossible. On the other hand, the Christian virtue of charity as a thing good in itself, and not necessarily to be practised as an insurance policy against purgatory after death, had important repercussions on the care of the poor and sick. At its height there developed a true brotherhood and spirit of sacrifice one for another which has never been seen to the same extent since that time. It showed itself particularly in the organisation of infirmaries and hospitals associated with the great monasteries, and in the development of the male and female nursing orders, both military and secular, which did such impressive work for the sick during the Middle Ages.

The Reformation destroyed the last remnants of these brotherhoods in England, and the commercial age began. From that time, measures to protect the public health were passed mainly as a means of self-preservation. Hospitals were developed *pour encourager les autres*. Thus, St. Bartholomews' Hospital was, in the 16th century, a place wherein the sick poor might remain, and if need be die, "which else might have died and stoncke on the eyes and noses of the Citie."

It is true that the first Public Health Act had been passed in 1388 and that the beginnings of a Ministry of Food had appeared early in the 16th century with the setting up of a central corn administration on London Bridge; but the lack of public opinion, combined with the ignorance of all classes, prevented any real progress. Meanwhile, there had been a steady development of commerce and the "covetous and insatiable cormorants" of Sir Thomas More became more and more a dominating factor in English life. About the year 1760 the invention of power-driven machinery came to their aid and thus began what has been described as the Industrial Revolution. It was of course merely an industrial acceleration. Many descriptions abound of conditions among the working classes of that time. Thus in one mill known as "Hell Bay" the workers for two months worked every day from 5 A.M. to 9 P.M., in addition to working all night twice a week. The growth of factories led to an ever-increasing demand for labour, and about 1760 the London poor-law authorities sent 20,000 children, of the average age of seven, to work in the mills and factories of Lancashire, Derbyshire, and Nottinghamshire. These children worked the same hours as the adults for six days a week, and on Sundays from 6 A.M. until noon they cleaned the machinery. A special strapper was usually employed to keep them at work. Similar conditions of child labour prevailed in the mines.

These appalling conditions led to the beginnings of modern social reform 150 years ago. The first Factory Act was passed in 1802 and the second in 1819; this limited the hours of work for those under sixteen years of age to a twelve-hour day with one hour overtime; but it was not until 1833 that the salaried factory inspector and the certifying surgeon appeared.

From the beginning of the last century the efforts of the reformers were supported by the trade unions and the coöperative societies and by an ever-growing body of public opinion. This public opinion arose from mixed motives of genuine pity and self-interest. It was this aspect of self-interest which Chadwick played upon so forcibly and effectively.

THREE STAGES

Our modern health services have developed since that time in three stages.

The first was concerned with environmental hygiene—such matters as the disposal of excreta, the purity of water-supplies and food-supplies, the abatement of overcrowding, better provision of air and light, and the control of infectious disease. The peak was reached with the great Public Health Act of 1875 and the results of this and allied Acts began to appear in full measure toward the end of the 19th century.

The next stage was the development of personal health services and arose from a different cause. After the Boer War an Inter-Departmental Committee on Physical Deterioration was set up, and its report, together with the reverses of the Boer War and the low standard of physique of the recruits thereby revealed, led to speedy action. Statutes to provide for a school medical service, to improve the maternity and child welfare services, and to introduce a limited form of national insurance were all in existence before the outbreak of the first world war in 1914. The subsequent extension of these services and the care devoted to the prevention and treatment of the venereal diseases and tuberculosis are too well known to require description.

The third stage is now in progress. This century has seen three great wars and remarkable and costly advances in medicine, surgery, and allied sciences. Finally the recent war has expedited a social and financial revolution. As a result the last few years have seen comprehensive social legislation placed upon the statute-book. To give only some examples, the Education Acts of 1944 and 1946, the National Insurance Act, the National Assistance Act abolishing the Poor Law, the Disabled Persons Act, and the Children Act form part of this comprehensive legislation. For medical services these Acts depend on the National Health Service Act of 1946. This is described in the preamble as an Act to provide for a comprehensive health service for England and Wales, and it is indeed comprehensive in its scope.

THE FUTURE

It may, therefore, fairly be claimed that the social machinery is almost complete. The citizen has now security, a healthy environment, and a long expectation of life. Infant mortality—that sensitive index of the national health—shows an 81% improvement since 1910 for the last three months of the first year of life. It may be asked, therefore, what remains to be done.

There are two main tasks. The first is to improve the existing services to their maximum degree of efficiency. This is in essence a matter of coördination. To give only one example, hospital, local-authority, and general-practitioner services require to be closely coördinated if an efficient and economical service is to be provided for the patient. The second task is to educate the people to use these services wisely and unselfishly.

There are, of course, a number of immediate problems to be dealt with. Thus the arrangements for the care

* Inaugural lecture delivered on Feb. 12 in a course arranged by the Central Council for Health Education.

Digitized by Google

of the premature infant need to be improved. The problem family requires to be tackled energetically. Efficient home nursing and home-help services must be built up. The care of the aged and infirm must be made better. Preventive, curative, and industrial medical services need to be integrated. Accidents in the home must be prevented. Mental-health services require to be extended and preventive psychiatry must be studied.

It is clear that in this country, so far as our health services are concerned, we stand at the cross-roads. These services may be either abused or properly used. It is now possible for the individual citizen to drift through life with little personal effort from the cradle to the grave. Alternatively he can, if he wishes, live the full life, dreamed by Aristotle, inspired by a consciousness of usefulness and purpose. An early development of the public conscience in these matters is imperative. Without it we shall merely follow the advice given in the Rubaiyat of Omar Khayyam:

> " How sweet is mortal sovranty " think some ;
> Others—" how blest the Paradise to come " ;
> Ah take the cash in hand and waive the rest ;
> Oh, the brave music of a *distant* drum !

THE ACTION OF DIHYDROERGOCORNINE ON THE CIRCULATION

WITH SPECIAL REFERENCE TO HYPERTENSION

R. H. GOETZ

M.B. Cape Town, M.D. Berne

RESEARCH ASSOCIATE PROFESSOR OF SURGERY IN THE UNIVERSITY OF CAPE TOWN

From the Department of Peripheral Vascular Diseases, Groote Schuur Hospital, Cape Town

THE beneficial results of sympathectomy in some cases of hypertension have stimulated research on drugs capable of paralysing sympathetic activity. Though the rôle of the sympathetic nervous system in the pathogenesis of hypertension is not quite clear, the contention that it plays an important part, at least in maintaining the high blood-pressure if not in its pathogenesis, has received new impetus from recent experiments. There is sufficient reason for trying to relieve hypertension by biochemical means directed towards interruption of excessive neurogenic constrictor influences on the vascular tree as a whole.

DIHYDROERGOCORNINE

Though crude ergot preparations had been used, particularly in obstetrics, for a long time, it was not until Barger and Carr (1906) isolated ergotoxine that a reliable crystalline ergot preparation became available which lent itself to exact pharmacological studies. Dale (1906) was the first to show that ergotoxine not only exerted an oxytocic effect but also directly constricted peripheral blood-vessels and other smooth muscles, and inhibited the sympathetic nervous system. He assumed that the sympathicolytic action was directed exclusively towards the terminal augmentor fibres of the sympathetic nerves.

Stoll and Hofmann (1943) showed that ergotoxine is not a single chemical substance but a mixture of three alkaloids—ergocornine, ergocristine, and ergokryptine. Smith and Timmis (1932) and Jacobs and Craig (1935, 1938) showed that all ergot alkaloids contain lysergic acid as a characteristic constituent. Stoll and Hofmann (1943) showed that one double bond of lysergic acid can be easily hydrogenated, yielding new chemical substances with definite chemical and pharmacological properties. Rothlin (1944, 1946), Stoll (1945), Bruegger (1945), Rothlin and Bruegger (1945), Spühler (1946), Imfeld (1946), and Orth and Ritchie (1947) proved these new hydrogenated alkaloids to be less toxic, less emetic, and more sympathicolytic, with less direct constrictive effect on smooth muscle.

Of the four hydrogenated ergot alkaloids dihydroergotamine (D.H.E. 45), dihydroergocornine (D.H.O. 180), dihydroergocristine, and dihydroergokryptine—I deal mainly here with dihydroergocornine, mentioning other compounds and other sympathicolytic drugs only to compare their effects.* Various reports of the effects of these drugs have been published already from this laboratory (Bluntschli 1947, Bluntschli and Goetz 1947a and b, 1948, Goetz 1947) or are in the press.

METHODS AND MATERIAL

Except those few tests which had to be carried out in the ward, all the examinations were done in a noiseless room with the person reclining quietly on a couch. The blood-pressure was determined at short intervals by clinical methods for an hour or longer to establish the basal pressure (Alam and Smirk 1943) before the drug was given. Dihydroergocornine was given either by slow intravenous injection at a rate of 0·1 mg. per min., or by intravenous drip lasting 15–30 min. as described elsewhere Goetz (1948a) :

> Two intravenous drips are set up, connected via a two-way tap to the needle. One drip is connected to an ordinary 'Vacoliter' and the other to a calibrated pipette containing 1 mg. of the drug in 50 ml. of saline solution. The test is started by giving intravenous saline solution, recording the blood-pressure, and getting all readings stabilised, whereupon the drug is given by turning the tap. Thus psychic disturbances in blood-pressure and peripheral blood-flow usually occurring with intravenous injections can be avoided, which obviously is important in investigations of this nature.

In a large number of investigations, dihydroergocornine was given intramuscularly, subcutaneously, by mouth, and (lately) intramuscularly in oil. Continuous records of the peripheral circulation were obtained with our optical digital plethysmograph (Goetz 1935, 1940, 1943, 1946). For the tests in the ward a portable model, with two pipettes for simultaneous recording of the blood-flow in two extremities (Goetz 1948b), was used. In many cases the respiration and skin temperatures were recorded simultaneously with the plethysmogram. On the plethysmogram the rate of arterial inflow and the heart-rate were continuously recorded.

The drug was administered to 37 persons with normal blood-pressure and 40 patients with hypertension. In every subject at least two tests were carried out, usually more, and to some hypertensives the drug was given for weeks or months. Of the hypertensives, 16 were retested after they had undergone subtotal sympathectomy (removal of the splanchnic nerves and the sympathetic chain from $D_{3(2)}$ to L). In addition the drug was tested in 16 patients with spastic vascular disease (Raynaud's phenomenon and acrocyanosis). Of the persons with normal blood-pressure and the patients with spastic vascular disease 21 had sympathectomies in one or more extremities, and some were tested before and after sympathectomy. Though it is realised that for the appraisal of the blood-pressure effects of any new drug the tests should be carried out under basal conditions, from the therapeutic point of view it is just as important to follow up the effects under ordinary outpatient conditions, which was done in several cases.

Dosage.—The largest single dose given intravenously to a person with normal blood-pressure was 1·25 mg., but the usual dose was 0·3–1·0 mg. intravenously to persons with normal blood-pressure, and 0·1–0·5 mg. to hypertensives. Apart from the fact that the hypertensives proved more sensitive to the drug (Bluntschli and Goetz 1947a and b), the sensitivity to

* I am indebted to Prof. E. Rothlin, head of the pharmacological department, Sandoz Research Laboratories, Basle, Switzerland, who kindly supplied us with those drugs which are not yet available commercially.

Digitized by Google

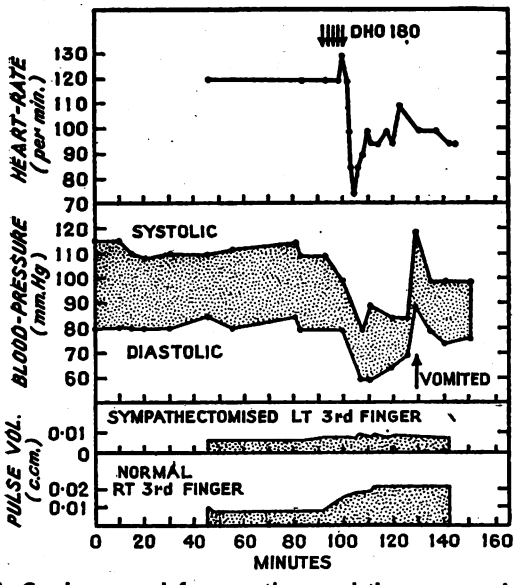


Fig. 1—Graph prepared from continuous plethysmogram, showing effect of intravenous dihydroergocornine 0·5 mg. on heart-rate, blood-pressure, and peripheral blood-flow in normal and in sympathectomised limbs. Note vasodilatation in normal right third finger and complete inertia of blood-flow in sympathectomised left third finger. Stellate and 2nd and 3rd dorsal ganglia had been removed two months previously for Raynaud's phenomenon. This dose proved somewhat too large and caused nausea. Patient vomited once, when blood-pressure rose (arrow).

D.H.O. 180 varied considerably from person to person. A dose which in one subject may be well tolerated and produce all the circulatory effects without any side reactions may produce nausea and vomiting in another subject. It is therefore essential to give first a small dose (0·1 mg.) and subsequently to increase the dose until the desired effect is obtained.

SIDE-EFFECTS AND TOXIC MANIFESTATIONS

Like all effects of the drug, the toxic manifestations do not follow immediately on injection but develop slowly within the next 10–15 min., often taking longer to appear. Subjectively, on administration of dihydroergocornine, the nose becomes stuffy and a slight headache may develop. Some patients feel tired. One patient became thirsty, one became hungry, and two had slight perspiration. Again, the dose causing these symptoms varied from person to person. With larger doses—e.g., 1 mg. in persons with normal blood-pressure and 0·5 mg. in hypertensives—nausea, vomiting, and epigastric pain may appear 15–30 min. after the injection.

Even well-tolerated doses of dihydroergocornine depress respiration. With larger doses the respiration becomes irregular and alarmingly slow. Circulatory collapse, such as we have observed after the administration of tetraethylammonium chloride, has never occurred after the administration of dihydroergocornine. One patient, in whom the drug was given as a therapeutic trial with good effect, developed difficulties in hearing, and he noticed a tapping sensation in the ears after receiving 1 mg. by mouth four times daily for 16 days (Bluntschli and Goetz 1947a). The blood-pressure at that stage was reduced to normal limits. In hypertensives even such small doses as 0·1 mg. injected intravenously may occasionally cause untoward side-effects such as nausea, but rarely vomiting. It made no difference to the side reactions whether the drug was given by intravenous injection or by intravenous drip.

EFFECT ON BLOOD-PRESSURE

In persons with normal blood-pressure dihydroergocornine, given intramuscularly, has no, or but a moderate, effect on the blood-pressure. Small doses (0·25–0·5 mg.) given intravenously produce a slight fall (10–30 mm. Hg) in both systolic and diastolic blood-pressure within 10–30 min. after the injection (fig. 1). This fall in blood-pressure is usually transient, lasting only from half to one hour, but may last two to three hours or more. With larger intravenous doses a temporary rise in blood-pressure of a similar magnitude has been observed in a few tests. However, in non-toxic doses a fall in blood-pressure is the rule. Again, it must be emphasised that it is difficult to compare the effects of a given dose in different people, since sensitivity to the drug varies. Possibly it is of importance whether we are dealing with a sympathicotonic or a vagotonic person. If the dose proves too big, there is the initial fall in blood-pressure; but, as nausea and vomiting develop, the blood-pressure rises temporarily (fig. 1).

In essential hypertension a fall in blood-pressure on small doses (0·2–0·3 mg.) of dihydroergocornine is constantly observed. A typical result is illustrated in fig. 2.

The patient was a woman, aged 53, who knew that she had had hypertension for at least twelve years. There was no renal, cerebral, cardiovascular, or endocrine disease to which the raised blood-pressure could have been secondary, and examination did not reveal any fundal or myocardial damage. The blood-pressure, taken in the outpatients' clinic, had always been about 240/140 mm. Hg, and at rest, before dihydroergocornine was given, the lowest reading was 200/105 mm. Hg. After the intravenous injection of dihydroergocornine 0·3 mg. the blood-pressure began to fall in 10 min. and reached 130/80 mm. Hg in 50 min. It remained at this level for about three hours, the patient feeling perfectly comfortable all the time. Thereafter it rose gradually to about 180/95 mm. On casual examination next day at the outpatients' clinic—i.e., twenty-four hours after the injection of the drug—the blood-pressure was 180/110.

In this case the blood-pressure was definitely lower twenty-four hours after injection of the drug than at

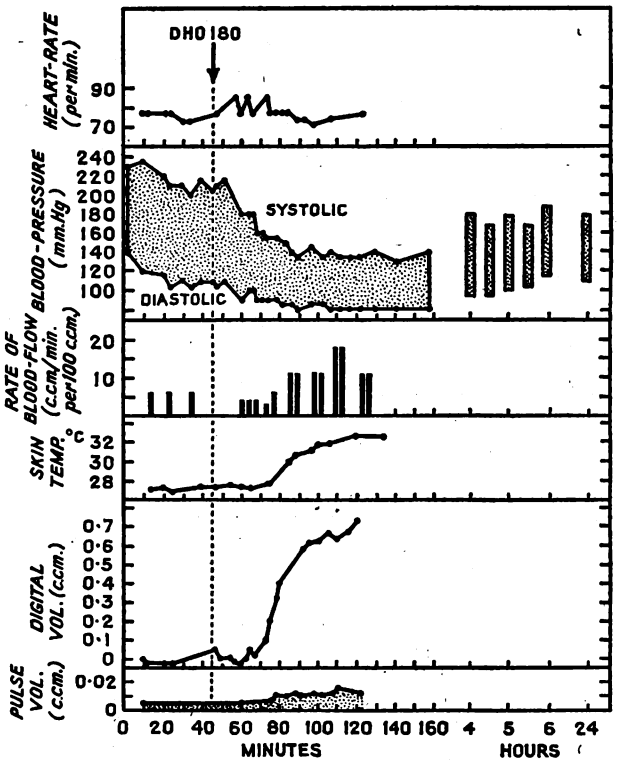


Fig. 2—Graph prepared from continuous plethysmogram, showing effect of intravenous dihydroergocornine 0·3 mg. on heart-rate, blood-pressure, rate of blood-flow (right first toe), digital volume (right first toe), pulse volume (right first toe), and skin temperature (right second toe) in essential hypertension. Note lower blood-pressure after 24 hours from single injection.

Digitized by Google

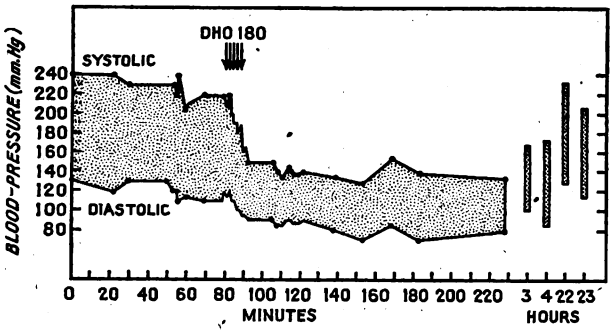


Fig. 3—Effect of intravenous dihydroergocornine 0·5 mg. on blood-pressure in arteriosclerotic hypertension.

any other time on casual reading at the outpatients' clinic. Indeed, in many of our hypertensives it was found that two or three days after the injection the blood-pressure was still lower than before (fig. 4). This strongly suggests that dihydroergocornine may be beneficial in hypertension. There is no definite relation between the action of the drug on the blood-pressure and on the heart-rate, and the blood-pressure may drop considerably without the heart-rate being affected.

Fig. 3 is a chart of the blood-pressure readings in a case of typical arteriosclerotic hypertension.

This patient hardly responded at all to dihydroergocornine 0·3 mg., but after 0·5 mg., given at a rate of 0·1 mg. per min. intravenously, the blood-pressure dropped from 240/120 to 150/90 mm. Hg within 15 min.; 70 min. after the injection 130/70 was recorded. The blood-pressure was still at this level two and a half hours after injection of the drug, when the patient was discharged, only to return three hours later with a blood-pressure of 170/110. Another four hours later the blood-pressure was 175/85 but next day it had returned to its original level.

Even in malignant hypertension it was possible to reduce the blood-pressure transiently to normal values.

Fig. 4 refers to a patient who had typical malignant hypertension with grade-III fundi, myocardial disease, and paroxysmal nocturnal dyspnœa, and had repeated attacks of hypertensive encephalopathy. Her blood-pressure was relatively fixed around 250/130 mm. Hg. After four spaced intravenous injections of dihydroergocornine 0·1 mg. the blood-pressure gradually dropped to the unbelievable level of 110/75 (fig. 4). Three hours after the injection it had returned to 170/80, but it remained about this level for a further five hours. Next day the highest blood-pressure reading was 190/100 and during the next two days the blood-pressure remained at this level. Thereafter the blood-pressure gradually returned to its original level—i.e., 250–240/130.

This is another example where, after an acute transient drop, the blood-pressure remained lowered for a considerable time, being higher than the lowest level in the acute drop but considerably lower than the original blood-pressure before the test.

Naturally, the question arose whether it would be possible to keep the blood-pressure depressed for weeks or months by giving an initial injection followed by a maintenance dose. For this purpose intramuscular injections of dihydroergocornine in oil were given, but we have not yet come to any definite conclusions or a definite scheme for therapy. In hospital it has been possible in this way to keep the blood-pressure depressed for weeks, but in general practice with ambulant patients a reliable method has not yet been worked out.

EFFECT ON PULSE-RATE

Dihydroergocornine in non-toxic doses as a rule depresses the heart-rate (figs. 1, 4, and 5). This depression, however, has never been of any consequence in any of our tests and it has never been such as to be called an untoward or toxic symptom. This is in sharp contrast to the cardiac acceleration caused by tetraethylammonium bromide, which in our experience has a most unpleasant and disturbing effect on the patient. Though blood-pressure and heart-rate usually drop simultaneously, the blood-pressure does not depend on the heart-rate, and in many tests there has been no definite relation between the effect of dihydroergocornine on the two. In numerous tests a considerable fall in blood-pressure has been observed without any effect on the heart-rate, as is well illustrated in fig. 2. The reverse also holds good; a fall in heart-rate being observed occasionally without a commensurate drop in blood-pressure.

EFFECT ON PERIPHERAL CIRCULATION

The effect of dihydroergocornine on the peripheral circulation does not bear any strict relation to the changes observed in blood-pressure or in heart-rate. In particular, the fall in blood-pressure does not depend on peripheral vasodilatation. In some subjects who were not fully dilated at the commencement of the test the peripheral blood-flow did not change at all, as judged by plethysmographic and skin-temperature readings, though there was a considerable drop in heart-rate and blood-pressure. In others there was a moderate dilatation (fig. 2). A few reacted with a stormy vasodilatation, and the pulse volume and rate of blood-flow reached their maximum vasodilatation level rapidly and remained there as long as two hours or even longer. A typical example is shown in figs. 1 and 5. As can be seen, in this test the blood-flow of the two upper limbs was recorded simultaneously.

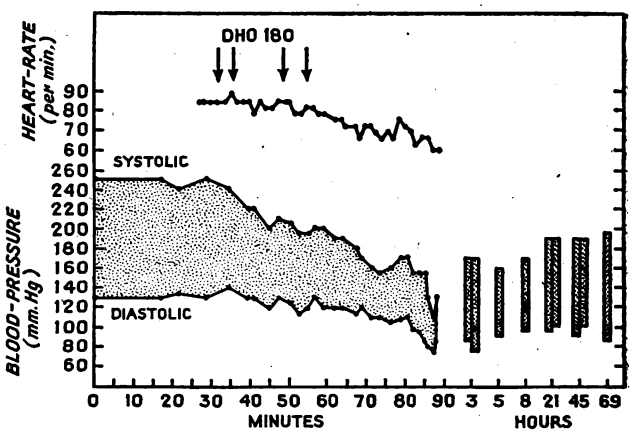


Fig. 4—Effect of intravenous dihydroergocornine 0·4 mg. on cardiovascular system in malignant hypertension. Note reduction in blood-pressure even after 69 hours from a single injection.

The vessels in the right limb were under normal sympathetic control, those of the left limb having been sympathectomised. Referring first to the normal right limb we note that after the injection of dihydroergocornine 0·5 mg. there was immediate vasodilatation, leading eventually to full vasodilatation (fig. 1). The pulse volume increased from 0·007 to 0·02 ml. within 20 min. (fig. 5) and remained at that level during the rest of the test. The skin temperature in that limb rose, in consequence, from 24 to 35°C. The rate of blood-flow, measured by the venous-congestion test (Goetz 1943, 1946, 1948b), increased eight times.

In the sympathectomised limb there was no change in the blood-flow after the injection of dihydroergocornine (fig. 1). The difference is even more striking on the original film (fig. 5). The pulse volume remained the same throughout the test, and what changes are recorded are due to the change in heart-rate. By comparing the effects on the normal and the sympathectomised limbs, simultaneously recorded, we can conclude that the

Digitized by Google

vasodilator effect of dihydroergocornine on the peripheral circulation depends on the integrity of the sympathetic nerve-supply. We are therefore dealing with a sympathicolytic effect, vasodilatation being the result of central inhibition of vasomotor tone.

In this connexion it is interesting to note that in our experience dihydroergocornine is of no use in the treatment of migraine. We have observed several patients who reacted well to ergotamine tartrate but did not respond to dihydroergocornine. This supports the contention of Graham and Wolff (1938) that it is the constrictor component in ergotamine tartrate which is responsible for the beneficial effect of this drug in migraine.

DISCUSSION

Though the sympathicolytic effect of ergot was demonstrated by Dale (1906), little if any therapeutic use could be made of this, since in all ergot preparations containing this principle it was coupled with a powerful direct effect on smooth muscle. The drugs therefore contained two principles which in their action on the vascular tree were competing with each other, the one being vasoconstrictor and the other dilator. Even more recently developed ergot derivatives—e.g., dihydroergotamine (D.H.E. 45)—which originally were thought by some workers (Rothlin 1944, Spühler 1946, Stoll 1945, Imfeld 1946) to contain only one principle, contained both the vasoconstrictor and the sympathicolytic principles (Rothlin 1946, Bluntschli and Goetz 1948). In isolating ergometrine chemists had succeeded in offering an ergot derivative with purely oxytocic action. In contrast, dihydroergocornine is the first ergot derivative with purely sympathicolytic action and hence is the true counterpart of ergometrine.

Like most sympathicolytic drugs, dihydroergocornine has a powerful effect in reducing blood-pressure; but, in contrast to others, particularly tetraethylammonium chloride, this is coupled with a fall in heart-rate. The effect of dihydroergocornine on the peripheral circulation is not so constant as its effect in reducing the blood-pressure; in fact it is unpredictable. The effect, if present, is always dilator and depends on the integrity of the sympathetic pathways; therefore it is truly sympathicolytic. The fall in blood-pressure produced by dihydroergocornine does not depend on peripheral vasodilatation and is observed in the absence of any reaction in the peripheral vascular bed. However, from unpublished experiments on animals we know that dihydroergocornine produces dilatation in the splanchnic bed, which suggests that dilatation in the visceral area plays an important rôle in the lowering of the blood-pressure by the drug. There is evidence that in man also the power of dihydroergocornine to lower the blood-pressure depends on the integrity of the sympathetic nerve-supply in the splanchnic area. After sympathectomy and high transverse spinal lesions the fall in blood-pressure due to dihydroergocornine is greatly diminished or absent. In a patient with a transverse lesion at D_3 there was a fall in heart-rate but none in blood-pressure. This is easily explained by the fact that the highest outflow from the spinal cord to the splanchnic area usually arises from D_5, and therefore in this patient the splanchnic bed was completely disconnected from the higher sympathetic centres. It therefore seems that dihydroergocornine acts on the sympathetic centres either in the medulla or in the hypothalamus.

Though the acute drop in blood-pressure usually lasts not more than a few hours, in many cases a definitely lower blood-pressure is observed one or two days after a single injection of dihydroergocornine. This offers definite therapeutic possibilities for the use of the drug in the daily management of hypertension. The hypertensive, however, tolerates smaller doses only. It is well to remember that he seems to be sensitive to the drug. This is well illustrated in one of our cases of malignant hypertension where the blood-pressure fell considerably after a minute amount of dihydroergocornine, which would be expected to cause hardly any reaction in a person with normal blood-pressure. The fact that patients with malignant hypertension should respond at all with a fall in blood-pressure to a sympathicolytic drug is of considerable interest. It supports the contention of Gregory and his colleagues (Gregory et al. 1943, Gregory and Levin 1945), who showed that even in patients with malignant hypertension and extreme structural arteriolar disease the rise in blood-pressure was due to increased vasomotor tone. They showed that in these cases high spinal anæsthesia lowered the blood-pressure considerably. In this connexion it is interesting that malignant hypertension often responds particularly well to splanchnicectomy.

Of all sympathicolytic drugs on which reports have been published and which have been tested by us, dihydroergocornine produces the least untoward side-effects in doses which lower the blood-pressure considerably. Tetraethylammonium chloride paralyses all autonomic ganglia—i.e., sympathetic as well as parasympathetic—and therefore partly acts like atropine, producing dryness of the mouth, loss of accommodation, increase of heart-rate, and interference with intestinal motility, all of which

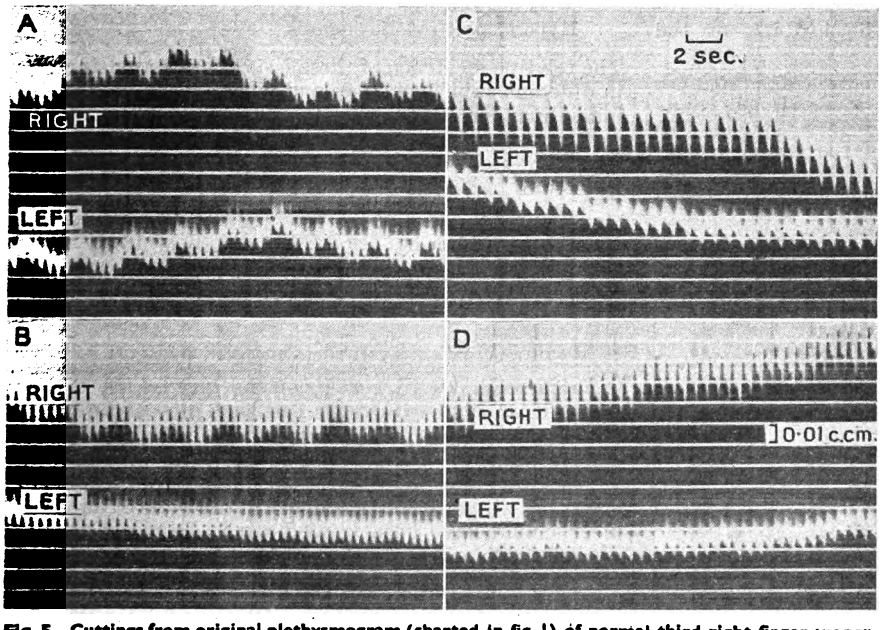


Fig. 5—Cuttings from original plethysmogram (charted in fig. 1) of normal third right finger (upper tracing) and of sympathectomised third left finger (lower tracing) simultaneously recorded with portable plethysmograph. A, before administration of dihydroergocornine, showing pulse volume equal in both digits (± 0·007 c.cm.). B, during injection of dihydroergocornine, showing immediate dilatation in normal (right) finger, its pulse volume being ± 0·012 c.cm. C, 18 min. after commencement of injection showing pulse volume of 0·02 c.cm. in normal limb and of 0·007 c.cm. in sympathectomised limb. Note full vasodilation in normal limb and lack of response in sympathectomised limb; drop in heart-rate. D, 140 min. after injection showing vasodilatation still present in the normal limb but effect on heart-rate wearing off.

Digitized by Google

militate against its extended use. Serious circulatory collapse has been reported and in one of our patients was observed after the injection of 100 mg. only. The systolic blood-pressure dropped rapidly from 240 mm. Hg to 60, and the heart-rate increased to 120–130. Though the patient eventually proved none the worse for this unfortunate reaction, it was an alarming experience.

In contrast to tetraethylammonium chloride, dihydroergocornine seems to exert a specific paralysing action on the sympathetic (adrenergic) system in the narrow sense, similar to the specific action of atropine on the parasympathetic (cholinergic) component of the autonomic nervous system. It therefore has none of the side-effects of tetraethylammonium chloride. The side-effects of dihydroergocornine produced by therapeutic doses, such as blocking of the nose, and tiredness, are few and inconsequential and cause the patient no distress. With toxic doses, however, nausea, vomiting, lassitude, and depression of respiration develop, and a rise in blood-pressure has been observed as well. These toxic symptoms seem to be due to a direct central effect.

SUMMARY AND CONCLUSIONS

The effects of the new hydrogenated derivative of ergot (dihydroergocornine, or D.H.O. 180) on the cardiovascular system are described.

Dihydroergocornine is purely sympathicolytic and does not contain the principle which acts directly on smooth muscle and is so characteristic of other ergot derivatives.

Dihydroergocornine lowers the blood-pressure considerably and decreases the heart-rate. These effects are constant, but the effect on the peripheral circulation is unpredictable; if present it is always vasodilator.

Hypertensive patients are more sensitive to the drug than are persons with normal blood-pressure. The possibilities of the drug in the management of the hypertensives are discussed.

Experiments on both man and animals indicate that vasodilatation in the cutaneous bed is not essential for the lowering of the blood-pressure with dihydroergocornine; but the splanchnic area seems to be important.

Evidence is presented to indicate that dihydroergocornine acts centrally, either in the medulla or the hypothalamus.

I am indebted to the J. S. Marais Research Fund and the Council for Scientific and Industrial Research for grants towards the expenses incurred in these investigations. To the members of the honorary staff of the Groote Schuur Hospital, who permitted the study of patients under their care, and to the doctors in private practice, who referred patients, I extend my thanks.

REFERENCES

Alam, G. M., Smirk, F. H. (1943) *Brit. Heart J.* **5**, 152.
Barger, C., Carr, F. H. (1906) *Chem. News*, **94**, 89.
Bluntschli, H. J. (1947) *S. Afr. med. J.* **21**, 21.
— Goetz, R. H. (1947a) *Ibid*, p. 382.
— — (1947b) *Schweiz. med. Wschr.* **77**, 769.
— — (1948) *Amer. Heart J.* **35**, 873.
Bruegger, J. (1945) *Helv. physiol. pharmacol. Acta*, **3**, 117.
Dale, H. H. (1906) *J. Physiol.* **34**, 163.
Goetz, R. H. (1935) *Pflüg. Arch. ges. Physiol.* **235**, 271.
— (1940) *Brit. J. Surg.* **27**, 506.
— (1942) *Clin. Proc.* **1**, 103.
— (1943) *S. Afr. J. med. Sci.* **8**, 65.
— (1946) *Amer. Heart J.* **31**, 146.
— (1947) *S. Afr. med. J.* **21**, 2.
— (1948a) *Lancet*, **1**, 830.
— (1948b) *S. Afr. med. J.* **22**, 391, 422.
Graham, J. R., Wolff, H. G. (1938) *Arch. Neurol. Psychiat.* **39**, 737.
Gregory R., Levin, W. C. (1945) *J. Lab. clin. Med.* **30**, 1037.
— Lindley, E. L., Levine, H. (1943) *Tex. Rep. Biol. Med.* **1**, 59, 167.
Imfeld, J. P. (1946) *Schweiz. med. Wschr.* **76**, 1263.
Jacobs, W. A., Craig, L. C. (1935) *J. biol. Chem.* **108**, 595; **110**, 521; **111**, 455.
— — (1938) *J. Amer. chem. Soc.* **60**, 1701.
Orth, O. S., Ritchie, G. (1947) *J. Pharmacol.* **90**, 166.
Rothlin, E. (1944) *Helv. physiol. Acta*, **2**, 48.
— (1946) *Schweiz. med. Wschr.* **76**, 1254.
— Bruegger, J. (1945) *Helv. physiol. Acta*, **3**, 519.
Smith, S., Timmis, G. H. (1932) *J. chem. Soc.* p. 763.
Spühler, O. (1946) *Schweiz. med. Wschr.* **76**, 1259.
Stoll, A. (1945) *Experientia*, **1**, 250.
— Hofmann, A. (1943) *Helv. chim. Acta*, **26**, 1570.

IMMEDIATE RESULTS OF PARTIAL GASTRECTOMY FOR PEPTIC ULCER

B. B. MILSTEIN
M.B. Lond., F.R.C.S.
ASSISTANT SURGICAL REGISTRAR, SURGICAL UNIT, UNIVERSITY COLLEGE HOSPITAL, LONDON

THIS investigation comprises an analysis of all cases of partial gastrectomy performed in the surgical unit of University College Hospital from 1940 until September, 1947. During this time 101 partial gastrectomies were done for the following conditions:

Peptic ulcer (without pyloric stenosis)	72
Organic pyloric stenosis (non-malignant)	28
Hypertrophic pyloric stenosis	1
Total	101

SELECTION OF CASES

All patients who were presented for operation with one of the indications in table I were operated on. No patients were refused operation on the grounds of age or because they were poor risks for other reasons—in fact, table III shows that many "poor risks" with various complicating conditions were included. The ages at operation range from the second to the seventh decade. The mean age at operation in 35 cases of gastric ulcer was 49·8 years (S.D. = 8·0), and in 44 cases of duodenal ulcer 42·4 years (S.D. = 9·0). The sex distribution was 15 females to 86 males, a ratio of 1 : 5·7. Among the females there were 9 gastric ulcers (ratio of 1 : 3·2) and 5 duodenal ulcers (ratio 1 : 8·0), the remaining case being one of hypertrophic pyloric stenosis. The reason for the preponderance of males is not known, but the series is small.

The type of lesion present at operation in these cases was as follows:

Gastric ulcer	38
Duodenal ulcer	45
Gastric and duodenal ulcer	6
Pyloric ulcer	7
Anastomotic ulcer	5
Hypertrophic pyloric stenosis	1

The relative incidence of these lesions varies considerably in different published series and must depend on different indications for operation in the minds of both physicians and surgeons.

Pyloric stenosis was present in 28 of these cases. It was found in association with:

Gastric ulcer in	6 cases
Duodenal ulcer in	16 „
Pyloric ulcer in	3 „
Gastric and duodenal ulcer in	2 „
Anastomotic ulcer in	1 case

DURATION OF SYMPTOMS BEFORE OPERATION

Table II shows that 20% of the gastric ulcers were operated on when symptoms had been present for a year or less, whereas only 2 duodenal ulcers were operated on as early as this. The cases of gastric ulcer were those in which carcinoma was suspected clinically. The table does suggest, however, that many of the cases of duodenal ulcer should have been treated surgically earlier. Only a few of the patients presented late; many had been under medical treatment for years, especially those who ultimately developed pyloric stenosis. There does not seem at present to be any way of distinguishing early those cases in which medical treatment will not prevent recurrences.

PREOPERATIVE COMPLICATIONS

The presence of complications before operation has an important bearing on postoperative mortality and mor-

Digitized by Google

bidity. In a few cases other diseases, such as tuberculosis and diabetes, were present, but most of these complications are directly or indirectly due to the gastric or duodenal lesion and its effects. These include obstruction, alkalosis and uræmia, gastrocolic fistula, previous operations causing adhesions which make gastrectomy more difficult and hazardous, and severe bleeding at the time of operation. Except in the cases of acute hæmorrhage, operation was delayed to treat these complications. Perhaps the commonest complication is activity of the ulcer, which leads to œdema, fixation, and vascular adhesions. Whenever activity of the ulcer was suspected, at least three weeks' rest in bed preoperatively on a suitable gastric diet was insisted on, and it is thought that this is one of the factors responsible for the low mortality recorded. The preoperative complications are shown in table III.

Of the 4 patients operated on for acute hæmorrhage 1 had had two previous perforations, his operation for hæmorrhage following two weeks after the second operation; and 1 had had severe hæmorrhage from an ulcer

TABLE I—INDICATIONS FOR OPERATION (102 OPERATIONS IN 101 CASES)

Indications for operation	Type of ulcer				
	Gastric	Duodenal	Pyloric	Gastric and duodenal	Anastomotic
Intractability, recurrence after medical treatment or repeated hæmatemeses ..	14	27	1	2	4*
Pyloric obstruction	6	16	3	2	1
Emergency operation for hæmorrhage	2	2	0	0	0
Cancer suspected	13†	0	3	2	0
Hour-glass contracture ..	4	0	0	0	0
Total ..	39	45	7	6	5

* Pylorectomy only in 1 case.
† Case of hypertrophic pyloric stenosis included.

while being prepared for suture of a burst abdomen ten days after an operation for intestinal obstruction due to adhesions. Both these patients recovered. Of the patients who had had previous operations for perforation 2 had undergone gastro-enterostomy at that time. Both presented with anastomotic ulcers.

OPERATION

The operation performed was in all cases a partial gastrectomy, with anastomosis of the gastric remnant to the jejunum. In the earlier cases about three-quarters of the stomach was excised; in later cases the resection was more extensive and devascularisation more complete. The anastomosis was a retrocolic, no-loop, anisoperistaltic, end-to-side or part end-to-side gastrojejunostomy. No Hofmeister valve was made. In 8 cases the pyloric exclusion operation of Finsterer was performed, the antral mucosa being stripped out in only 2. There have been minor variations in technique, but three principles have been observed throughout:

(1) In mobilising the stomach, mass ligature of tissues has been avoided, vessels being ligated separately or in small groups.

(2) No clamps have been used except on edges of gut that were subsequently invaginated—i.e., the duodenal stump and the lesser curve of the stomach for the part end-to-side anastomosis.

(3) All closures and anastomoses were made in two layers: (*a*) a continuous all-coats suture of catgut; and (*b*) interrupted seromuscular sutures of fine serum-proof silk.

TABLE II—DURATION OF SYMPTOMS BEFORE OPERATION (76 CASES)

Duration of symptoms	Gastric ulcer	Duodenal ulcer
Under 6 mos.	5	0
More than 6 mos. but less than 1 yr.	2	2
1–5 yr.	13	14
6–10 yr.	6	12
11–15 yr.	3	9
16–20 yr.	2	1
Over 20 yr.	3	4
Total	34	42

No great care was taken to avoid peritoneal soiling, gross spilling of gut content being prevented by suction. Sulphanilamide was sometimes dusted on the peritoneum when soiling was not controlled as when the ulcer floor was left in situ. The peritoneum was closed with catgut, the linea alba or rectus sheath with serum-proof silk, and the skin with thread. The peritoneum was not drained.

The importance of any detail in the technique is not easy to determine, and any attempt to attribute the low mortality-rate and absence of complications from leakage to technical details would be merely speculative. The adoption of the three principles described prolonged the operation to 2–2½ hours. With modern anæsthesia, prolonging an operation to this extent probably has no adverse effect in itself, but it does increase the risk of infection, if only by prolonging the opportunity for contamination. With a meticulous suture technique the chances of glove puncture are increased, and it has already been shown from this unit [1] that the surgeon's hands can be a potent source of wound infection. The only modification of technique made in the light of the experience of this series is the closure of the abdominal wound with stainless steel wire throughout.

Postoperative Treatment

Intermittent gastric suction through a Ryle tube placed in position before operation was maintained until the gastric fluid balance became positive. Fluids were permitted after six hours, and the diet rapidly increased so that the patient was taking a Meulengracht I diet on the seventh day and Meulengracht II on the ninth. The lack of complications from distension or obstruction is thought to be due to the routine use of gastric suction in the early postoperative period.

TABLE III—PREOPERATIVE COMPLICATIONS

Complications related to ulcer	No. of cases	Complications unrelated to ulcer	No. of cases
Previous perforation	14	Pulmonary tuberculosis ..	2
Bleeding at operation (emergency) ..	4	Diabetes mellitus	2
Pyloric obstruction ..	28	Intrathoracic tumour ..	1
Hour-glass deformity	4	Intermittent hydronephrosis	1
Gastrocolic fistula ..	1	Tabes dorsalis	1
Other previous operations for ulcer ..	3	Renal and extrarenal uræmia	1
		Disseminated sclerosis and renal glycosuria ..	1
		Cystic bronchiectasis of left lung	1

Note.—5 cases had two complications each; 1 had three.

POSTOPERATIVE COMPLICATIONS

These are detailed in table IV. The incidence is excessive and gives cause for much concern. Most of these complications prolonged the patient's stay in hospital and his convalescence, increasing his loss of earning capacity and the loss of bed space for the hospital. They are nearly all preventable and from the point of view of both surgical practice and economics deserve further attention.

1. Devenish, E. A., Miles, A. A. *Lancet*, 1939, 1, 1088.

Digitized by Google

In an attempt to see whether the position had improved recently with the advent of chemotherapy and the practice of early ambulation and preoperative and postoperative exercises, the figures were analysed separately for the early and later groups of cases. These figures show that the incidence of complications as a whole has fallen from 61 to 39%, while pulmonary complications have been reduced to less than half. There has been no burst abdomen in the last 46 cases. The incidence of wound sepsis, however, is unchanged. The remaining complications in the recent series form a miscellaneous collection difficult to classify or interpret.

However, it is noteworthy that there was no gastric retention of any significance, and no secondary operations for obstruction were required. This is attributable partly to the suture technique but chiefly to the use of routine gastric suction in the first few postoperative days. Leakage from a suture line occurred in 1 case only. This complication is caused less by inadequate suturing than by tension at the suture line, usually due to gastric distension, and lack of attention to the preoperative nutritional state. Here again, adequate preoperative preparation and gastric suction are the important prophylactics.

Wound Infection

These infections were nearly all staphylococcal and therefore derived not from soiling with gastric and jejunal contents but from the surgeon's hands or possibly from the patient's skin. They sometimes arise deeply, with the result that an unexplained pyrexia with a normal-looking wound is present for days before local signs appear. The infection often surrounds the thread or silk sutures used to repair the linea alba. The presence of these foreign bodies leads to persistence of the infection, with discharging sinuses, until the sutures are removed or discharged, which in some cases takes six to nine months. In 3 cases at least, wound infection was responsible for a subsequent ventral hernia. The use of stainless steel sutures, which have been shown to excite no tissue reaction even in the presence of infection, is likely to shorten the period of disability from this complication.

TABLE IV—POSTOPERATIVE COMPLICATIONS (102 OPERATIONS)

Complication	All operations (102)*	Operations before January, 1945 (56)	Operations after January, 1945 (46)*
Superficial wound infection	15	9	6
Deep wound infection	2	1	1
Atelectasis	11	9	2
Pyrexia of unknown origin, cough, bronchitis	5	3	2
Burst abdomen	5	4	1†
Bronchopneumonia	2‡	0	2‡
Subhepatic abscess	2	0	2
Lung abscess	2	2	0
Pulmonary embolus	2	2	0
Peritonitis	1‡	0	1‡
Persistent hiccup	1	0	1
Femoral thrombosis	1	1	0
Postoperative gastric bleeding	1§	1	0§
Postoperative melæna	1	0	1
Dysentery, bloody diarrhœa	2	1	1
Penicillin rash	1	0	1
Hydropneumothorax	1‖	0	1‖
Tension pneumothorax and congestive cardiac failure	1‖	0	1‖
Pressure palsy of arm	1	0	1
Empyema	1	1	0
Total complications	58	34	24
Total cases with complications	52 (61%)	34 (61%)	18 (39%)

* 4 cases had two complications each; 1 had three.
† Skin only.
‡ One death each.
§ Operation for hæmorrhage (also included as subhepatic abscess).
‖ Followed intercostal block.

TABLE V—ANÆSTHETIC COMPLICATIONS (83 CASES)

Complication	Type of anæsthetic: Local (24)	Gas, oxygen, and ether (38)	Spinal and epidural (7)	Curare with inhalation anæsthesia (14)
Atelectasis	2	5	1	2
Pulmonary embolus	1	1	0	0
Lung abscess	0	2	0	0
Pneumonia	0	1	0	1
Cough, pyrexia of unknown origin, &c.	0	3	1	0
Pneumothorax	2	0	0	0
Empyema	1	0	0	0
Total	6	12	2	3

The problem of eliminating wound contamination is very difficult, since glove punctures are very frequent during gastrectomy, especially with the particular suture technique used in this series. Until a suitable method is found which will prevent access of organisms to the wound, chemical prophylaxis with local application of penicillin to the wound layers during closure may diminish the incidence of infection.

Anæsthetic Complications

The complications in table IV which are possibly referable to anæsthesia have been further analysed, according to the anæsthetic technique, in table V. This shows apparently that the greatest incidence of these complications was when gas, oxygen, and ether were used. However, further consideration suggests that this is far more an indictment of anæsthetists than of anæsthetics, since the least experienced anæsthetists were the most likely to use gas, oxygen, and ether. The advantages of control of the diaphragm while dissecting at the œsophageal end of the stomach, and when dealing with the left gastric artery and coronary vein, give curare an important place in anæsthesia for gastrectomy; and, since the anæsthetic complications from curare in this small series are no more frequent than those from other agents, its place is assured.

MORTALITY

There were 2 deaths in the 101 patients in whom 102 operations were performed—a mortality-rate of 2%. Details of these 2 cases are as follows:

Case 1.—A woman, aged 35, had an anastomotic ulcer and pyloric stenosis. She also had a macrocytic anæmia of unknown origin, and had been under medical treatment in hospital on an ulcer diet for three months before operation. She made satisfactory progress until the fifth postoperative day, but then went downhill rapidly and died on the eighth postoperative day from general peritonitis due to a leak at the "Y" suture line (end-to-side jejunal anastomosis). This was confirmed at necropsy, which also showed that the scar in the abdominal wall had not begun to heal. This death was attributed to insufficient attention to the patient's preoperative nutritional state.

Case 2.—A man, aged 54, had pyloric stenosis, disseminated sclerosis, and renal glycosuria. He was undernourished and wasted and would be classed as a poor operative risk. The operation was difficult, and the base of the ulcer was left in the pancreas. The operation was fairly well tolerated. After operation there was a gradual rise in pulse-rate, and eighteen hours after the operation the patient suddenly collapsed. He was given an infusion of 2 pints of blood, and recovered. Examination of the chest, abdomen and wound, and the electrocardiogram were all negative. Two days later the patient collapsed again and died suddenly.

Necropsy showed bronchopneumonia of the lower lobes of both lungs, and a satisfactory operation site with no sign of hæmorrhage. The pathological findings did not explain the clinical state before death, and the cause of the collapse remains unexplained.

Digitized by Google

DISCUSSION

These 102 operations were performed by eight different surgeons, as follows:

Senior surgeon	.. ..	63 operations, 1 death
First assistant	.. ..	25 operations, 1 death
Six registrars	.. ..	14 operations, no deaths
Total	.. ..	102

Hence the results cannot be said to be those of one expert alone and therefore beyond the scope of the average general surgeon. They are to be attributed rather to the following of a routine in operating which involves careful hæmostasis, accurate closure of the duodenal stump and construction of the anastomosis, the preparation of the patient by prolonged rest and attention to the nutritional state, and the use of postoperative suction.

The immediate operative mortality in this series is 2%. None of the 4 patients operated on in emergency for hæmorrhage died, though 3 of them were aged over 50. This is to be attributed to the liberal use of blood-transfusions, which renders the operation as safe as when there is no active hæmorrhage, though it is complicated by the activity of the ulcer, which is nearly always penetrating.

SUMMARY

Among 101 consecutive partial gastrectomies for peptic ulcer performed by eight members of the surgical unit of University College Hospital the mortality was 2%.

In contrast to the low mortality there was a high morbidity-rate, complications being recorded in 51%.

The low mortality is attributed to preoperative rest, strict suture technique, and postoperative gastric suction, and was maintained in spite of the inclusion of many bad-risk cases.

Among many complications, infection, which occurred in 17%, stands out as the most frequent and the most amenable to prevention.

AGRANULOCYTOSIS AND THROMBOCYTOPENIA FOLLOWING THE USE OF TRIDIONE

T. W. FORSTER M.B. Lond.
J. W. WATSON M.B. Lond.
HOUSE-PHYSICIANS TO THE PÆDIATRIC UNIT
E. NEUMARK M.B. Lond.
LECTURER IN PATHOLOGY
ST. MARY'S HOSPITAL AND MEDICAL SCHOOL, LONDON

'TRIDIONE' (3, 5, 5-trimethyloxazolidine-2, 4-dione) was first investigated as an anticonvulsant by Everett and Richards (1944) and Thorne (1945). Lennox (1945) found it effective in the treatment of the epilepsies, and after further study he reported (Lennox 1947) that it was more effective in idiopathic than in organic forms, and that the best results were obtained in the petit-mal triad, the effects in most cases being confirmed by changes in the electro-encephalograms. Of his 166 patients, with many seizures daily not controlled by other drugs, 83% were improved by treatment with tridione—31% being free from seizures for from one to fifteen months, 32% continuing with less than a quarter the number of seizures, and 20% being slightly improved; 13% were unchanged and 4% showed an increase in the number of seizures. Lennox found that tridione was ineffective in grand mal and in other forms of convulsions.

Lennox reported several side-effects. Of his 222 patients 122 developed symptoms which could be attributed to tridione, but only three effects were considered important: photophobia, rash, and neutropenia. Photophobia, hemeralopia or "glare," was the commonest, occurring in 68 patients, but was not often observed in children under six years of age. Lennox could offer no explanation for the phenomenon and found nothing abnormal on ophthalmological examination. In 2% of his patients it was sufficiently severe to require withdrawal of tridione.

A rash developed in 32 patients, mostly young children. It took two distinct forms: (1) more commonly, acneiform papules or small shot-like nodules in the skin of forehead or face; and (2) a generalised morbilliform rash in 5 patients (2%). He disregarded the former but took the latter as an indication to discontinue treatment immediately. In most cases the rash then disappeared and treatment with tridione was resumed.

The third side-effect, neutropenia, shows, as Lennox points out, the associated effects of drug allergy on the skin and the hæmopoietic system, as seen with sulphonamides. In his series, 127 patients on tridione for several months up to two years, all controlled by monthly blood-counts, showed no significant decrease of hæmoglobin, red cells, or platelets, but in 6% the neutrophils fell to 1600 per c.mm. or less. After discontinuation of tridione in these patients the blood-count returned to normal, and in most cases the treatment was then restarted. Lennox took a fall of leucocytes to 4000 per c.mm. with less than 40% neutrophils, or less than 1600 neutrophils per c.mm., as an indication to stop treatment, at least as a temporary measure. Lennox also mentions one other patient on tridione who died from aplastic agranulocytic anæmia and bleeding which could not be checked. In this case and in 2 others personally communicated to him the blood had not been examined. Davis and Lennox (1947) studied the effects of tridione on the blood and found that in 13% of their 245 patients the neutrophils were reduced to less than 2000 per c.mm. They suggested that tridione should not be given to patients with a family history of blood dyscrasia or allergy, and insisted that the blood must be examined monthly. If the neutrophils fell to less than 2500 per c.mm., blood-counts were to be done more frequently; and, if they fell to 1600 per c.mm., tridione was to be withdrawn.

Harrison et al. (1946) reported a case of fatal aplastic anæmia following the use of tridione and hydantoin in a girl of sixteen with grand mal. Her hæmoglobin fell to 7·6 g. per 100 ml., polymorphs were only 6% of 1000 white cells per c.mm., and the platelets numbered only 42,000 per c.mm. At necropsy the bone-marrow was hypoplastic, and there were hæmorrhages in the spleen, kidneys, and bladder.

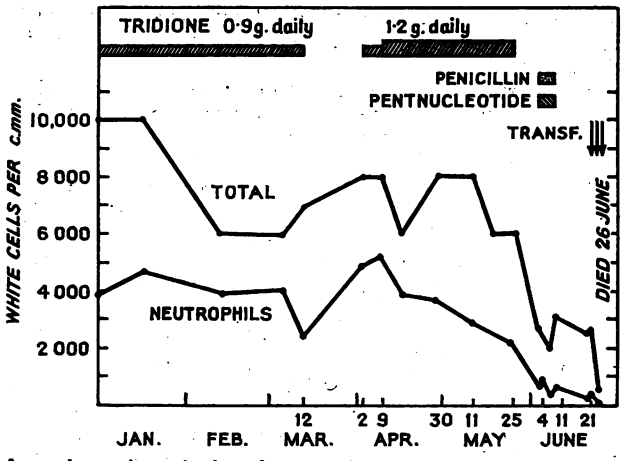
Mackay and Gottstein (1946) saw a case of aplastic anæmia and agranulocytosis in a woman of twenty-three who had been on tridione for ten months. She had anæmia, neutropenia, and thrombocytopenia, but bone-marrow biopsy showed an almost normal myelogram. At necropsy there were hæmorrhages in most of the internal organs.

Greaves (1946) reported a case in which neutropenia developed as a result of sensitivity to tridione. When treatment was stopped blood-counts returned to normal levels.

Complete agranulocytosis associated with tridione therapy was reported by Braithwaite (1948). A boy of eleven years developed an urticarial rash on the 25th day, and gingivitis and pyrexia on the 51st day, of treatment and died 21 days after tridione was discontinued. The hæmoglobin was 44%, the leucocytes were 800 per c.mm., polymorphs were not seen, and the platelets were normal. Sternal marrow biopsy showed "aplasia of erythroblastic tissue and primary agranulocytosis." At necropsy the bone-marrow was dark red, and sections showed some normoblastic hyperplasia but almost complete absence of myeloid elements.

Butter (1948) reported a group of 23 cases of petit mal treated with tridione. Glare was noted in 19 patients but it was only temporary. One case developed a slight acneiform rash, and in another a severe rash in the face, neck, and hands eventually turned into acute dermatitis. Neutropenia was not observed in this series.

Digitized by Google



Agranulocytosis and thrombocytopenia after use of tridione in epilepsy.

Briggs and Emery (1949) reported that of 10 cases of petit mal 3 developed neutropenia. In one of these, serial blood and marrow examinations were carried out. There was neutropenia, thrombocytopenia, and mild anæmia, and in the marrow the granulocytes and megakaryocytes were scanty. All values slowly returned to normal after cessation of tridione therapy.

CASE-RECORD

The following case illustrates a number of points raised by Lennox:

A schoolboy, aged eleven years, was an only child. There was no history of epilepsy, allergy, or migraine in the family or of birth injury. When he was five years old he fell from a bicycle on to his head. Six months later he began to have clonic spasms of the arms, each attack lasting a few seconds, after which he became pale and dazed for two minutes and then had a frontal headache for five minutes. He never vomited, grimaced, or lost consciousness in the attacks but occasionally was incontinent of urine. By the age of nine and a half the number of attacks had increased to 12 a day, and he was therefore referred to hospital in December, 1945. Owing to irregular schooling he was educationally backward.

Physical examination revealed no abnormality. Radiography of the skull was normal, and Wassermann and Kahn tests negative. Electro-encephalography showed general dysrhythmia, with the spike and wave pattern pathognomonic of epilepsy, but no focus of abnormality was seen.

After six months on phenobarbitone the patient still had 8 or 9 attacks a day. 'Epanutin' gr. $1^1/_2$ b.d., given since October, 1946, reduced the frequency of the attacks to 3 a day and improved him mentally and physically. In April, 1947, a "fixed gaze" and automatism followed some of the attacks. From Nov. 28, 1947, tridione 0·3 g. was given twice daily in place of epanutin, and regular blood-counts were made. After a week the dose was increased to 0·3 g. t.d.s. and supplemented by phenobarbitone gr. $^1/_2$ b.d. Within a fortnight the boy was free from attacks. Apart from a major attack in January, 1948, he was well and attending school regularly.

Tridione was discontinued on March 12, 1948, because a blood-count showed only 2400 neutrophils per c.mm. By April 2 the attacks were occurring again at the rate of 3 a day, and, a blood-count on that day having shown that the neutrophils had risen to 4500 per c.mm., tridione was restarted. On April 9 the dosage was increased to 0·3 g. q.d.s., and phenobarbitone gr. $^1/_4$ q.d.s. was given because the attacks were still uncontrolled. On April 30 a few acneiform spots appeared on the patient's nose and forehead, and they persisted until his death. On May 11 he complained of dazzle in bright sunlight. On May 25 the neutrophils were 2100 per c.mm., and so tridione was stopped. On June 4 there were only 700 neutrophils per c.mm. in a total white-cell count of 2700 per c.mm. (see figure). The patient was admitted to hospital and given 'Pentnucleotide' and systemic penicillin. There was no physical abnormality except the acneiform rash and slight injection of the fauces. On June 11 the patient was removed from hospital by his parents against medical advice. On June 21 he was severely ill with a sore throat and was readmitted. His temperature was 101·8°F, he had an ulcerated throat, severe gingivitis, and a generalised petechial rash.

A blood-count on June 22 showed Hb 90% (13·4 g. per 100 ml.), red cells 4,300,000 per c.mm., colour-index 1.0, mean cell diameter 7 μ, white cells 2600 per c.mm. (neutrophils 2%, eosinophils 2%, lymphocytes 95%, monocytes 1%), and platelets 40,000 per c.mm.

He was treated with systemic penicillin, pyridoxine, liver extract, vitamin-B complex, and vitamins C and K. On June 23 his gums were bleeding, and in the evening epistaxis started and continued for two days despite anterior and posterior nasal plugging. During that time a blood-transfusion of 2 pints of group-O blood was given. On June 25 the temperature suddenly rose to 104·8°F and the patient became confused. There was no evidence of this being due to the transfusion. The patient had a fixed gaze and occasional twitchings. He became incontinent of fæces and had abdominal pain and melæna. His temperature, pulse-rate, and respiration-rate rose steadily until he died on June 26.

Necropsy.—The body was that of a well-developed boy with generalised petechiæ and a large bruise in the left buttock region. Endocardial and pericardial petechiæ were present. The lungs showed confluent bronchopneumonia and basal congestion, with many small and a few larger hæmorrhages in the pleuræ and throughout the substance of the lungs. There were several ulcers with fibrinous sloughs in the pharynx and in the upper part of the œsophagus, many petechiæ in the stomach, and several hæmorrhagic areas in the mucosa of the ileum. In the liver the distribution of fat was patchy. The bone-marrow of the right femur, ribs, and vertebræ looked normal macroscopically. In the spleen, weighing 87 g., the malpighian bodies stood out well. Thymic remains floated in water. Lymph-glands were not conspicuously enlarged, but several abdominal lymph-glands had areas of hæmorrhage. Several discrete hæmorrhagic areas were seen in the bones of the vault of the skull. The other organs were normal.

Histology.—Femoral marrow showed only a few centres of hæmopoietic activity. Almost all the cells had compact round nuclei and basophilic cytoplasm, and were arranged loosely rather than in clusters. They were mostly lymphocytes, and there were a few myeloblasts. A few promyelocytes, myelocytes, eosinophil cells, and cells of the erythropoietic series were seen. Megakaryocytes were very scanty. Only occasional mitotic figures were seen. The marrow was grossly hypoplastic, almost aplastic. A few small hæmorrhages were seen in the interstitial tissue of the cortex and medulla of the kidneys. Spleen, heart, and lymph-glands were normal.

COMMENT

In this case, during tridione therapy acneiform spots appeared and were followed by dazzle, neutropenia, and thrombocytopenia. The number of neutrophils continued to fall after tridione was discontinued.

It is clear that regular and frequent clinical and hæmatological examinations are of great importance. Monthly examinations, as suggested by Lennox, do not seem to us sufficiently frequent, since a fall in the leucocyte-count, when it takes place, may be very rapid. A daily blood film, perhaps the ideal, is not always feasible in a large clinic. Following Whitby and Britton (1946), we agree that treatment with drugs which are potentially toxic to the bone-marrow should be stopped before the lower limit of normal of 1500 neutrophils per c.mm. is reached.

If the appearance of the acneiform rash, like that of the morbilliform type, is taken as an indication to stop tridione therapy, possible fatalities might be avoided.

It seems doubtful whether the taking of a drug should be resumed after a break, if once toxic effects on either skin or bone-marrow have been observed, unless such a patient is successfully "desensitised."

Our thanks are due to Dr. R. Lightwood and Prof. W. D. Newcomb for helpful criticism, and to Mr. H. N. Stafford, H.M. Coroner for the Western District, County of London, for permission to publish this case.

References at foot of next page

Digitized by Google

NECROTIC JEJUNITIS

K. A. FICK
M.D. Hamburg
PATHOLOGIST, ALSTERDORFER KRANKENHAUS, HAMBURG

A. P. WOLKEN
M.D. Berlin
CAPTAIN R.A.M.C.

IN general, both clinicians and pathologists tend to disregard the jejunum as the site of tumours and inflammations. It is therefore surprising to find an apparently endemic, severe, and often fatal affection of the jejunum, observed during the past few years in Northern Germany.

CLINICAL FEATURES

Though sometimes there is a short prodromal stage, the onset is usually acute, with violent pain in the upper abdomen. Often the pain is located a little to the left of the midline and is associated with a hyperæsthetic Head's zone from T7–T12 on the left side and a reflex rigidity of the abdominal wall in the same segments (Ruppert 1947). At the same time the patient usually suffers from nausea and vomiting. Apart from the severe pain in the upper abdomen, however, the most striking clinical feature is circulatory collapse due to toxæmia; this comes on at an early stage, and the patient may die in twenty-four hours after the onset of the first symptoms. Those who survive this stage pass into either a condition characterised by enteritis with bloodstained diarrhœa or a condition of intestinal obstruction resembling paralytic ileus. Occasionally both conditions occur together. The body temperature is about 38°C (100·4°F) and seldom rises above this, except with the appearance of specific complications. The erythrocyte-sedimentation rate (E.S.R.) is high. The leucocyte-count shows a less striking increase. The differential white count (Cooke-Arneth) shows a shift to the left, and considerable toxæmic changes are observable in the white cells. No definite changes in the urine have been noted. The gastric juice shows either normal or decreased acidity.

DIAGNOSIS

Certain radiological findings may perhaps prove significant: these include rigidity of the wall, defects of the mucosa, and formation of gas in the upper jejunum. In view of the severity of the disease, however, it is obvious that most of the patients should not be expected to undergo barium-meal radiography of the gastro-intestinal tract. The differential diagnosis includes other catastrophes of the upper abdomen (such as perforation, mechanical obstruction of the small intestine, and fatty necrosis of the pancreas) and is undoubtedly difficult in many cases. We have observed that large portions of the mucosa of the jejunum occasionally become separated, work their way into the intestinal lumen, and appear as bile-stained tissue shreds in the fæces.

TREATMENT

Surgical manœuvres, such as resection, exteriorisation, and the establishment of a fistula in the small intestine are recommended, particularly in severe cases; by these procedures some patients may be saved. Less severe cases, however, can be cured by conservative treatment aimed at replacing fluid loss and stimulating the peripheral circulation. The hypothesis that necrotic jejunitis is caused by an anaerobic organism has recently led Lezius of Lübeck to treat patients with large doses of sulphonamides (containing particularly 'Marfanil' and its derivatives, which have been found very effective in the treatment of anaerobic infections in Germany). The favourable results of this treatment, however, cannot easily be assessed owing to other treatment given at the same time.

PATHOLOGY

Macroscopic

Laparatomy or necropsy reveals a high degree of inflammation and necrosis of a more or less extensive section of the jejunum. This striking alteration in the small intestine starts abruptly, in most cases high up in the jejunum (in one case observed by us even immediately below the pylorus), and ends just as abruptly. Sometimes the jejunum shows several parts of its length altered in this way. Cases have been observed in which the altered tissue extended to the ileum, and even to the colon. In a case of necrotising enteritis observed by one of us during his early work at the Pathological Institute of the Allgemeines Krankenhaus, Altona, Germany, the lower third of the œsophagus was in condition corresponding to the changes in the upper small intestine.

Specimens have been prepared by the resection, at operation, of the affected portions of the jejunum during an early phase of the disease; they are curiously sausage-like in appearance, rigid, and with a bright red serosa bearing vertical striations. This peculiar rigidity of the small intestine is due to œdema of the intestinal wall, which may become so thick that the lumen is almost closed. This narrowing of the lumen might in itself explain the obstruction which is such a frequent feature. However, a better explanation of the obstruction is that the wall of the affected part of the jejunum remains inactive during peristalsis. In a case of recent jejunitis seen at operation the mucosa looked as if it had been severely cauterised. At a later stage complete necrosis of the mucosa develops (fig. 3), and finally parts of the mucosa or submucosa slough, often leaving extensive ulceration. Where the disease is protracted, peritonitis may follow, by direct extension of inflammation through the intestinal wall; but some other cases have ended dramatically in perforation. Major, and sometimes fatal, hæmorrhages may take place, especially in the later stages. Even if the patient survives the jejunal necrosis his life may still be threatened by its after-effects. Thus scar stenoses and dense peritoneal adhesions have been observed, leading to mechanical obstruction.

Unlike those in the small intestine, changes in the other organs are slight. Moderate swelling of the mesenteric lymph-glands is seen occasionally. The larger parenchymatous organs show hardly any changes, and never advanced inflammation, though hæmorrhagic foci have been found (Baniecki 1947, Jeckeln 1947).

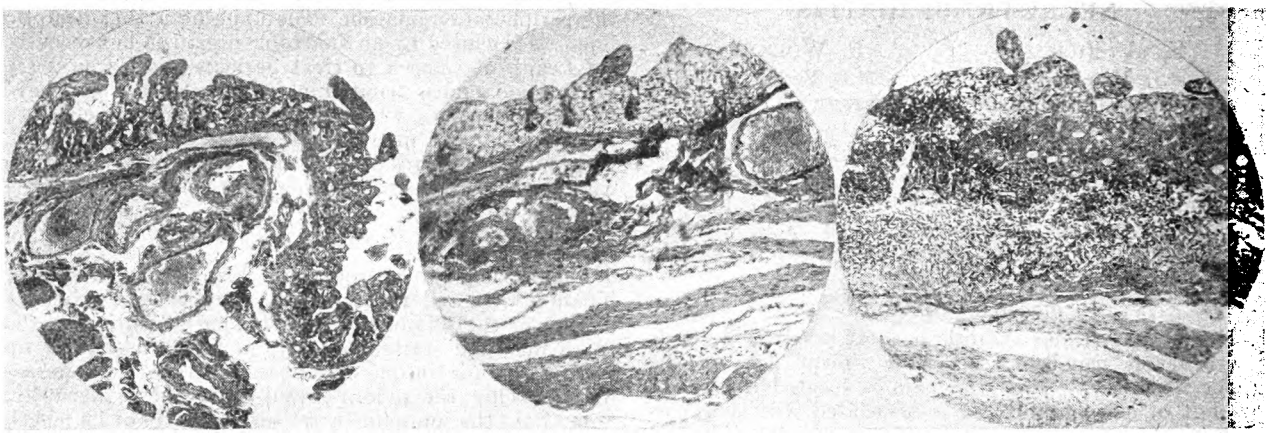
Histology

The histological picture in the gut is that of fairly generalised necrosis, the degree of which varies with the resistance of the different tissues and the duration of the illness. In early cases the necrosis is limited to the mucosa (figs. 1 and 2), suggesting that the cause comes from the lumen of the intestine. The submucosa is the main site of the œdema mentioned above, as would be expected from the looseness of its texture. This œdema often seems to be hæmorrhagic owing to the early disintegration of the vessel walls by necrosis. The necrosis, penetrating the mucosa at a given place, occasionally gives the impression of spreading particularly rapidly in the submucosa; at the same time the mucosa in other areas, as well as the muscularis, remains intact

DR. FORSTER AND OTHERS: REFERENCES

Braithwaite, R. F. (1948) *Brit. med. J.* i, 14.
Briggs, J. N., Emery, J. L. (1949) *Lancet*, Jan. 8, p. 59.
Butter, A. J. M. (1948) *Brit. med. J.* i, 13.
Davis, J. P., Lennox, W. G. (1947) *J. Pediat.* 31, 24.
Everett, G. M., Richards, R. K. (1944) *J. Pharmacol.* 81, 402.
Greaves, R. J. (1946) *J. Amer. med. Ass.* 132, 44.
Harrison, F. F., Johnson, R. D., Ayer, D. (1946) *Ibid*, p. 11.
Lennox, W. G. (1945) *Ibid*, 129, 1069.
— (1947) *Ibid*, 134, 138.
Mackay, R. P., Gottstein, W. K. (1946) *Ibid*, 132, 13, 163.
Thorne, F. C. (1945) *Psychiat. Quart.* 19, 686.
Whitby, L. E. H., Britton, C. J. C. (1946) Disorders of the Blood. 5th ed., London.

Digitized by Google



(1) (2) (3)

Fig. 1—Early stage of necrotic jejunitis, showing œdema and early necrosis of villi and severe hyperæmia of submucosa.

Fig. 2—Later stage of necrotic jejunitis, showing severe œdema, increased necrosis of mucosa, early inflammatory infiltration, and increased hyperæmia of submucosa.

Fig. 3—Late stage of necrotic jejunitis, showing total necrosis of mucosa and severe inflammation of submucosa, with beginning separation of necrotic tissue.

for a comparatively long time. This process mainly takes the form of a pure necrosis while inflammation subsides. In only a few cases was there a great invasion of leucocytes leading to suppuration. For this reason some pathologists refuse to regard this disease as an inflammation and look on the cellular infiltration as a secondary manifestation. But various necrotic inflammations have been described, and by close comparison with them we consider the term "jejunitis" justified—a view fully shared by most pathologists familiar with the disease. In all advanced cases the serosa is also involved and shows a fibrinous inflammation. Gram-stained sections reveal many varieties of organisms near the lumen, especially in the necrotic mucosa, but only sparse clusters of bacteria in the deeper tissues. Despite many investigations of this kind, we have not discovered any single or even predominant causal organism in the pathological tissues of the intestinal wall.

A NEW DISEASE?

In any attempted explanation of the nature and cause of necrotic jejunitis the first question to arise is whether this is a new disease or not. Some clinicians and pathologists deny any connexion between this condition and sporadic suppurative processes of the jejunal wall that have been hitherto described. Others are inclined to identify particularly the phlegmon of the duodenal or jejunal wall with necrotic jejunitis. A study of the previous literature, however, reveals that the occasional cases of suppuration of the jejunal wall recorded from time to time include entirely different diseases. In opposition to the views of others, we see no connexion with regional ileitis, which Crohn et al. (1932) have regarded as a "closed" form of disease; we think a sharp distinction should be made between the two. Moreover, necrotic jejunitis is certainly distinct from diseases of the wall of the small intestine distinguished in their primary stages by pronounced suppuration and proved to originate by way of the blood-stream.

There remain, however, a few published cases which correspond fully to the jejunitis seen today. But these are rare and sporadic cases. Necrotic jejunitis, occurring endemically, with characteristic clinical features and distinct pathological and anatomical findings, has not hitherto been described.

ÆTIOLOGY

Until the cause of this new disease has been established, the causal treatment and prophylaxis will be unknown. Many suggestions have been made but none has been proved. It is most widely thought that necrotic jejunitis is due to invasion of the intestinal wall by normally non-pathogenic bacteria when resistance is lowered. The cause most often held responsible for this weakened resistance is a general change and restriction of diet. Such a change must be considered as at least one factor in the pathogenesis of necrotic jejunitis; this is confirmed by the fact that cases described formerly as corresponding fully in pathology and anatomy to those noted above nearly all occurred at times characterised by a dietary change. It is also confirmed by Siegmund's (1926) experiments on animals, in which lethal *Salmonella enteritidis* infection was studied in starving rats; he concluded that the intestinal epithelia of starving animals became pervious to substances and bacteria which otherwise exist inoffensively in the intestinal lumen. However, it is doubtful whether the ætiology of necrotic jejunitis can be completely correlated with the effects of malnutrition; this has been attempted by Kloos (1946) but in many cases of jejunitis the patients gave no past history nor showed any physical signs of inanition, but on the contrary were adequately nourished. At any rate, it seems to be established that jejunitis is very often preceded by voluminous meals rich in cellulose.

According to another view, necrotic jejunitis is a specific infective disease. This view is supported by its endemicity in Northern Germany; its exclusive incidence during the summer months, which has been observed yearly since 1944 (Fick 1947); and the discovery, in a few cases where sections have been made, of metastatic hæmorrhagic foci in other organs, such as the testes and the spinal cord (Baniecki 1947, Jeckeln 1947). Hormann (1947) identifies a virus as the causal organism; Lippelt (1947) believes *Bact. coli hæmolyticum* to be responsible, and by feeding this bacterium, cultured from diseased human jejunum, to mice has produced in them a condition resembling human jejunitis. Schütz (1948) found repeatedly in the duodenal juice of patients with jejunitis anaerobes which he could not identify. With cultures of these germs lesions macroscopically and microscopically identical with those of human jejunitis were produced in guineapigs.

These various explanations are only a few of those advanced. It has even been suggested that this jejunal disease results from intestinal cauterisation by mustard gas, which has entered the patients' intestines from the consumption of Baltic Sea fish, which in turn have been contaminated by the wholesale destruction of gas ammunition in the Baltic.

Digitized by Google

We hold that the two chief theories of the origin of necrotic jejunitis can be readily combined. Thus, necrotic jejunitis is a specific infective endemic disease, to which defects in the diet predispose. These defects lower the resistance of the tissues of the intestinal wall and also alter the bacterial flora of the intestines.

PERSONAL CASES

In 1944–48 we observed eighteen cases of jejunitis in the hospitals of Altona and Alsterdorf. The patients were thirteen men and five women with an average age of 61 years. Sixteen of them died after an average duration of 7 days' illness. Two patients, a man aged 60 and a woman aged 49, were saved by resection of the affected parts of the jejunum. We have not observed any cases of jejunitis among relations, and, so far as we know, except for two cases in twins, none has yet been reported by other workers. We did not see any cases in children, such as other clinicians and pathologists have reported.

The following two cases are typical:

Case 1.—The illness of this man, 62 years old, started acutely with extremely severe pains in the upper abdomen. After a short time he developed diarrhœa and later started to vomit. Soon he felt extremely weak and could not arise alone. Two days after the beginning of the illness the diarrhœa stopped and now the condition resembled obstruction, with painfully swollen abdomen and frequent vomiting. At this stage the patient came into hospital.

On examination he appeared to be seriously ill and undernourished (he had lost nearly 25 lb. in weight during the past year). He had an anxious facies, with striking cyanosis. The pulse could hardly be felt, its rate being 124. Temperature 101°F. Leucocytes 16,000 per c.mm., E.S.R. 42 mm. in 1 hour and 87 mm. in 2 hours (Westergren). Hypo-acidity of the gastric juice. The abdomen was swollen and the upper abdomen especially sensitive to pressure.

Obstruction of the small intestine was diagnosed. Because of the severe circulatory collapse an operation could not be performed. The patient died twenty-four hours after he had entered hospital and four days after he had first complained of symptoms. Necropsy showed a fresh fibrinous peritonitis caused by an advanced necrotic and ulcerative jejunitis.

Case 2.—A merchant, aged 60, who had lost by undernourishment about 35 lb. during the last two years. Hypertension of 200/120 mm. Hg, observed two years ago, went down to 110/70 (symptom of undernourishment). The illness started with severe pains in the upper abdomen a little to the left of the midline. Next day the condition was worse and accompanied by severe hiccup. When the patient started to vomit bile from the small intestine he was sent to hospital. In the evening of the same day the surgeon diagnosed obstruction. Operation revealed the upper jejunum swollen and inflamed. The whole of the altered part (41 in.) of the small intestine was resected. The patient recovered slowly after the operation and was discharged in good health a few weeks later. The resected part of the intestine showed typical recent necrotic jejunitis.

SUMMARY

A jejunal disease of high fatality which has been increasing in incidence in Northern Germany since 1944 is described.

This disease is an endemic necrotic jejunitis with characteristic clinical and pathological findings.

It is thought to be a specific infection to which defects of diet predispose.

Since this paper was written a new bacillus has been discovered in the intestinal lumen in some cases of jejunitis by Prof. J. Zeissler, of Hamburg (Zeissler and Rassfeld-Sternberg 1949). This bacterium, previously unrecognised, is an anaerobe and belongs to the group of *Clostridium welchii*. It forms a powerful toxin. It is worthy of note that it is closely related to another bacillus, of the same group of *Cl. welchii*, which causes dysentery in lambs, a condition characterised by a severe enteritis. Zeissler holds that his organism, which he names *Cl. enterotoxicus* or *Cl. welchii* type F, plays an important part in the causation of jejunitis. It has also been found in healthy people in Northern Germany. Should further research confirm Zeissler's opinion about this organism, it will also confirm our opinion that necrotic jejunitis is a specific infection, whose manifestation depends on certain other factors.

BIBLIOGRAPHY

Baniecki H. (1947) *Hamburg. Ärztebl.* **1**, 39.
Beckermann, F., Laas, E. (1946) *Ärztl. Wschr.* **1**, 329.
Braun, H. (1942) *Zbl. Chir.* **69**, 1984.
Crohn, B. B., Ginzburg, L., Oppenheimer, G. D. (1932) *J. Amer. med. Ass.* **99**, 1323.
Edelhoff, J. (1947) *Dtsch. med. Wschr.* **72**, 228.
Fick, K. A. (1947) *Z. ges. inn. Med.* **2**, 447.
Frik, W. (1947) *Dtsch. med. Wschr.* **72**, 164.
Hormann, H. (1947) *Ärztl. Wschr.* **1–2**, 998.
Jeckeln, E. (1947) *Dtsch. med. Wschr.* **72**, 105.
Kloos, K. (1946) *Ärztl. Wschr.* **1**, 294.
Lezius, A. (1948) *Dtsch. med. Wschr.* **73**, 176.
Lippelt, H. (1947) *Hamburg. Ärztebl.* **1**, 40.
Meyer-Burgdorff, H. (1947) *Dtsch. med. Wschr.* **72**, 186.
Ruppert, C. (1947) *Ibid*, p. 108.
Schütz, F. (1948) *Ibid*, **73**, 176.
Siegmund, H., in Henke, F., Lubarsch, O. (1926) Handbuch der speziellen pathologischen Anatomie und Histologie. Berlin; vol. IV, p. 3.
Wilker, F. (1947) *Hamburg. Ärztebl.* **1**, 50.
Zeissler, J., Rassfeld-Sternberg, L. (1949) *Brit. med. J.* **1**, 267.

EFFECT OF INTRA-UTERINE RADIUM THERAPY ON OVARIAN FUNCTION

GERTRUDE GOLDSCHEIDER
M.D. Vienna, M.R.C.S.
CLINICAL RESEARCH OFFICER, MARIE CURIE HOSPITAL, LONDON

WOMEN at the climacteric have a high urinary output of gonadotropic hormone.

Zondek (1926) showed this by injecting their urine into immature female mice and thereby producing premature ripening of the ovarian follicles. The follicles of the mice became fully ripe but did not develop further, no corpus hæmorrhagicum or luteinisation being found. The precocious secretion of œstrin due to early ripening of follicles caused in turn early vaginal canalisation, cornification of the vaginal epithelium, and hypertrophy of the uterus. Zondek's findings were confirmed by Heller and Heller (1939). This reaction is known as the positive Aschheim-Zondek reaction 1 (A.Z.R.1).

The increase in the urinary output of gonadotropic hormone lasts for several months after the menopause is fully established. Later, according to Zondek (1931), the level reverts to normal, and remains there in 85% of women for the rest of their lives. Österreicher (1932), Saethre (1933), and Jones and MacGregor (1936), on the other hand, report that in old age it is persistently high.

Women who have not yet reached the climacteric excrete only small amounts of gonadotropic hormones, insufficient to ripen the follicles of mice. In such women the A.Z.R.1 is negative.

Nathanson et al. (1940) assessed the amount of gonadotropic hormones in the urine of 11 women who had been sterilised by irradiation of the ovaries (10 with X rays and 1 with radium). All showed an increase persisting for several months. These workers therefore concluded that an artificial menopause produced by irradiation was similar to the natural menopause.

However, in only 1 of their 11 cases was the castration effected with radium; and, as simple menorrhagia is now so often treated with a small intra-uterine dose of radium, I thought it desirable to ascertain whether the amenorrhœa following such treatment is of ovarian or non-ovarian origin. I have accordingly determined the urinary excretion of follicle-stimulating hormones in 28 women before and after intra-uterine treatment with radium for menorrhagia, and have compared the results with those obtained in a few patients who had been castrated with X rays or had received a combined course of X rays and radium.

Digitized by Google

TABLE I—URINARY EXCRETION OF GONADOTROPIC HORMONES IN RELATION TO INTRA-UTERINE RADIUM THERAPY FOR MENORRHAGIA

Case no.	Age (years)	Radium (m.e.h.)	Aschheim-Zondek reaction 1												
			Before treatment	Months after treatment											
				1	2	3	4	5	6	7	8	9	10	12	16	24
1	31	500	−	−	−	−	−	−	−	−	−	..	−	−	..	..
2	32	1000	−	−	−	−	−	..	−	Panhysterectomy						
3	32	600	..	..	−	−	..	−	−	..	−	..	..	−	−	..
4	32	1980	−	−	−	..	..	−	−	..	−	−	−	−	−	..
5	35	1050	−	..	..	..	..	−	..	?	?	?	−	−	..	..
6	37	1270	−	−	−	−	−	..	−	−	−	..	−	−	−	..
7	38	1100	−	−	−	−	−	−	−	..	−	..	..	−	..	..
8	39	1540	−	−	..	−	..	..	?	−	−	..	−	−	..	..
9	39	1100	−	−	−	−	..	−	..	..	−	..	..	−	..	..
10	40	1100	−	−	−	−	−	−	Lack of further coöperation							
11	41	1100	−	−	−	−	−	..	−	..	−	−	..	−	−	..
12	42	1100	−	−	−	−	−	−	..	−	−	−	..	..	..	..
13	43	1100	−	−	−	−	−	..	−	−	..	..	..	−	..	..
14	44	1276	−	−	−	−	..	−	..	..	−	..	..	−	..	..
15	44	1100	..	−	−	..	−	−	−	−	..	−	..	−	−	−
16	44	1540	..	−	−	−	..	−	−	..	−	..	−	−	−	..
17	45	1100	−	−	−	−	−	−	−	..	−	..	−	−	..	..
18	45	1100	−	−	..	−	−	−	−	..	−	Lack of further coöperation				
19	45	1270	−	−	−	..	?	−	..	−	..	−	..	−	−	..
20	45	1760	..	..	−	..	..	..	..	..	−	−	−	−	..	..
21	46	1100	+	+	+	..	+	..	..	+	+	..	+	..	−	..
22	46	1270	−	−	−	..	−	−	..	−	..	−	..	−	..	..
23	49	1100	−	−	?	..	−	−	..	−	−	−	..	−	..	..
24	50	1100	−	..	−	−	Lack of further coöperation									
25	52	1760	−	−	−	−	−	−	..	−	−	..	..	−	..	..
26	53	1276	−	..	−	−	−	−	−	−	−	..	..	−	−	..
27	53	1100	−	−	Lack of further coöperation											
28	54	1540	−	+	..	..	..	..	+	..	..	..	−	−	−	..

Of the 28 women 27 gave closely similar histories. The menstrual cycle had been regular until within a few months of treatment, when the periods became irregular and more frequent and the flow increased in amount and duration. Occasionally floodings had occurred. In 1 case only was there a history of amenorrhœa; this had lasted for several months before the onset of irregular and excessive menses. In 27 of the 28 cases histological examination of the curettings revealed a hyperplastic condition of the uterine glands. There was 1 case of endometrioma (table I, case 4).

METHOD

The original Aschheim-Zondek technique was used.

The freshly voided morning specimen of urine was filtered, acidified, and treated with tricresolum purum (1 drop to 25 ml.) The gonadotropic hormone was assessed in five female mice under four weeks of age and under 3 g. in weight. Each mouse received 0·5 ml. of the filtrate twice daily by subcutaneous injection for three consecutive days. A vaginal smear was taken 96 hours after the first injection if the vagina proved to be patent, after which the animals were killed with carbon monoxide. The reaction was reported as positive when the ovaries of at least two animals showed growth of the follicles, the accompanying vaginal reaction denoted œstrus, and the uterus showed engorgement and hypertrophy. In all positive cases sections of the ovaries were made to confirm the clinical findings microscopically. In positive cases the histological picture showed medium or large follicles. Many of them contained well-formed follicular cavities filled with follicular fluid. In many cases typical graafian follicles were present, but no corpus hæmorrhagicum or luteinisation was found. The uterus showed thickened endometrium and myometrium, and the epithelial cells lining the lumen had

TABLE II—URINARY EXCRETION OF GONADOTROPIC HORMONES IN RELATION TO IRRADIATION THERAPY FOR BENIGN UTERINE LESIONS

Case no.	Age (yrs.)	Diagnosis	Date of treatment	Intra-uterine radium (m.e.h)	Dose of X rays (r)				Aschheim-Zondek reaction 1													
					Left iliac region	Left sacral region	Right iliac region	Right sacral region	Months after treatment													
									1	2	3	4	5	6	7	8	9	10	To 12	To 16	To 24	Longer
29	33	Metropathia	— 1933	750	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			March, 1936	..	600	600	600	600	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			Nov., 1936	..	700	700	700	700	..	..	..	..	..	..	..	..	..	..	..	..	..	+
30	37	Endometrioma	June, 1942	770	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			July, 1942	..	600	600	1600	1600	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			Feb., 1943	..	1700	1700	1700	1300	+	..	+	..	+	+	+	..	..	+	−	−	..	..
31	37	Endometrioma	June, 1942	1170	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			June, 1943	1650	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..
			July, 1943	..	600	600	1700	1700	..	−	..	−	−	..	..	..	..	..	..	..	..	..
32	42	Fibroids	March, 1943	..	600	600	600	600	−	−	..	+	Lack of further coöperation									
33	44	Endometrioma	Sept., 1941	2310	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			Oct., 1941	2200	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			March, 1942	..	2100	2100	600	600	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			Aug., 1942	..	2000	2000	..	..	..	..	..	..	−	−	..	−	±	±	+	+	−	..
34	45	Menorrhagia; ? endometrioma	Oct., 1942	1100	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			Oct., 1942	..	1800	1800	..	..	..	..	..	..	+	..	..	+	+	+	±	−	−	−
35	47	Fibroids	April, 1943	..	600	600	600	600	..	±	..	..	+	..	−	−	−	−	..	..	..	..
36	49	Endometrioma	Feb., 1943	1980	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
			March, 1943	1980	..	..	..	..	+	+	±	..	+	..	−	+	..	±	+	+	−	..

Digitized by Google

become more columnar. The uterine glands were very well developed.

Before radium was given, the patient's urine was tested for follicle-stimulating hormones to exclude a pre-existent positive A.Z.R.1. This preliminary test could not be made in 4 of the 28 patients owing to the toxicity of the urine. The mice used for these 4 tests died before completion of the test, and there was no time to obtain a further sample before treatment.

In 23 cases the A.Z.R.1 was negative before treatment. The 1 patient who gave a positive A.Z.R.1 before treatment was aged 46 and had been amenorrhœic for several months before the irregular bleeding started. She seems to have reached the climacteric before the onset of the investigation. Owing to the positive A.Z.R.1 before treatment the case was considered unsuitable for the investigation and was omitted from the final results.

The dosage of radium in this series was 600–1900 mg. element-hours (m.e.h.). Women of child-bearing age were usually given the smaller doses, and in menopausal cases the usual dose was about 1100 M.e.h. After the radium treatment the urine was assessed as a routine for follicle-stimulating hormones at regular intervals for at least twelve months wherever the patient would coöperate.

RESULTS

In 22 patients the A.Z.R.1 was continuously negative throughout the period of observation (table I). Of the remaining 5 women 3 produced a doubtful positive reaction on one occasion, and in 1 other a doubtful positive reaction persisted for three months. Only 1 patient developed a positive A.Z.R.1 immediately after treatment. Aged 54, she was the oldest in the group. It is well known that the ovaries in older women are more easily inactivated by irradiation, the follicles being less numerous and probably less active. In a woman of menopausal age it is therefore not surprising that a small dose of radium may sometimes establish the climacteric.

The radium treatment cured the menorrhagia in 27 of 28 patients. In the remaining case hysterectomy was necessary.

With the disappearance of menses there was no further clinical evidence of cyclic activity. The absence of an increase of follicle-stimulating hormones in the urine of these patients suggests strongly that an artificial menopause had not been established, and that the amenorrhœa following treatment was of non-ovarian origin; it was produced presumably by destruction of the uterine glands, the function of the ovaries remaining intact.

Intra-uterine application of radium for the treatment of menorrhagia is sometimes deprecated on the ground that it produces an artificial menopause. This study of 28 cases, however, suggests that so long as only small doses are given this result need not be feared.

COMPARISON WITH X-RAY CASTRATION

In 8 patients (table II) complete sterilisation was considered advisable. These had either endometrioma or fibroids. They were sterilised either with X rays alone or by combined treatment with intra-uterine radium and deep X rays to the ovaries.

Sterilisation was usually achieved with a dose of 600 r to the skin over each of four areas, two anteriorly and two posteriorly, the treatment being spread over twelve days (kV 190, mA 6, distance 60 cm., filter 1 Cu, 1 Al). Larger doses were given only to patients with endometrioma. Some of the patients received one or two further courses of treatment within twelve months (table II).

In patients with endometrioma sterilisation was the treatment of choice. In those with fibroids sterilisation was adopted only when operation was contra-indicated and intra-uterine radium inadvisable because of the large size of the fibroids.

In no case of this series was the urine examined before treatment. After treatment the urinary gonadotropic output was high and the A.Z.R.1 was positive and remained so for several months. This finding confirms the conclusion of Nathanson et al. (1940) that X rays can produce a real menopause. Case 36 (table II) may suggest that the same result can be obtained with large intra-uterine doses of radium, but in this case the radium dosage was at least three times as large as the average menorrhagia dose.

SUMMARY

The dose of intra-uterine radium usually given at the Marie Curie Hospital for benign menorrhagia, though capable of producing amenorrhœa, does not produce an artificial menopause, except in women of menopausal age, where such small doses may influence their ovarian function.

Irradiation of the ovaries with X rays establishes the menopause.

I wish to acknowledge my indebtedness to Dr. Mary Gilmour for her advice, and to the British Empire Cancer Campaign and the Medical Research Council for their support.

REFERENCES

Heller, C. G., Heller, E. J. (1939) *J. clin. Invest.* **18**, 171.
Jones, M. S., MacGregor, T. N. (1936) *Lancet*, ii, 974.
Nathanson, I. T., Rice, C., Meigs, J. V. (1940) *Amer. J. Obstet. Gynec.* **40**, 936.
Österreicher, W. (1932) *Klin. Wschr.* **11**, 813.
Saethre, H. (1933) *Ibid*, **12**, 140.
Zondek, B. (1926) *Z. Geburtsh. Gynäk.* **90**, 372.
— (1931) Die Hormone des Ovariums und des Hypophysenvorderlappens. Berlin.

USE OF THROMBIN IN LIVER PUNCTURE

L. FRIEDRICH M.D.
M. POLICZER M.D.
ASSISTANT PROFESSOR

From the 2nd Internal Department of the Korányi Hospital, Budapest

THE greatest risk in liver puncture is hæmorrhage. Sherlock[1] found a mortality of 0·67% in 1200 cases (264 of her own and 936 collected from reports published by other workers). In her last 138 punctures, however, there had been no evidence of hæmorrhage. Numerous procedures have been suggested to prevent bleeding. Sherlock allows the patient 24 hours' rest in bed and has the pulse-rate and blood-pressure measured every hour; if hæmorrhage is diagnosed, a blood-transfusion is given without delay. She opposes the injection of drugs into the site of the puncture on the grounds that it adds to the time taken by the biopsy and thereby increases the risk of tearing the liver. Nevertheless, after satisfying ourselves that it did no harm to the liver tissue in the cadaver, we have adopted a method in which commercial thrombin is injected into the needle-track after the biopsy specimen has been withdrawn. The thrombin is provided in powder form by the Servita Laboratory under the name 'Citostat.' The solvent, put up in separate phials, contains pyrocatechin and calcium chloride to enhance

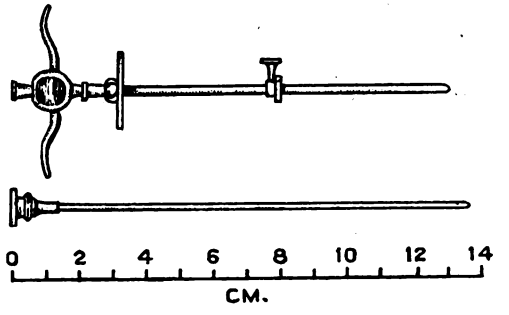


Fig. 1—Inner and outer components of liver-puncture needle.

1. Sherlock, S. *Lancet*, 1945, ii, 397.

Digitized by Google

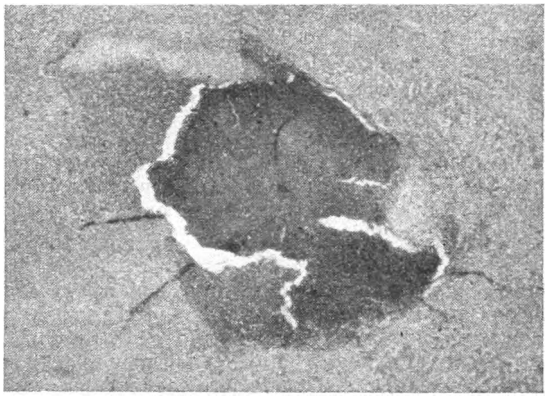


Fig. 2—Necropsy specimen of site of liver puncture, a week after puncture, showing partially organised thrombus after injection of thrombin at time of puncture.

thrombin activity, and sodium chloride and tricresol to ensure sterility and stability. We have obtained the best effects with a solution containing 200 coagulation units in 1 ml. of solvent. A clear solution cannot be obtained, because traces of fibrin are present to form coagulation foci and hasten coagulation.

The liver-puncture needle we use (fig. 1) is double, the outer needle being 12 cm. long and 2 mm. in bore, the inner 1·4 mm. in bore and fitted with a stylet. The outer needle is graduated in centimetres and a depth-screw is provided to control the depth of the puncture.

The procedure is as follows:

Bleeding-time, clotting-time, and in cases of jaundice prothrombin-time also, are measured and the blood-group is determined beforehand. On the day of biopsy the patient has no breakfast and is given an enema. Puncture is performed with the patient in the recumbent position, slightly inclined to his right side (this is especially important if ascites is present). The patient's right arm is placed under his head. The puncture is usually made in the anterior or posterior axillary line in the 9th or 10th intercostal space according to the results of radioscopy. If the liver is enlarged or tumour nodules are palpable, transperitoneal puncture from in front is preferred. After outlining the liver by percussion and marking the place where the needle is to be passed, the skin is painted with iodine. With a hypodermic needle a weal is then raised with 2–4% procaine, and the hypodermic needle is next passed through the pleural cavity as far as the peritoneum. At this moment pain is felt. The patient is asked to take a deep breath, whereupon the needle is felt to be rubbing the liver surface. The peritoneum and the liver surface are next anæsthetised. The hypodermic needle is withdrawn to measure the distance between skin and liver surface. The regulating screw on the liver-puncture needle is adjusted to allow the needle to be passed 2–3 cm. deeper than the hypodermic needle was. It would be dangerous to pass it deeper, because 4–5 cm. below the capsule there are rather large branches of the portal vein. After an interval of 10–15 min. the patient takes a deep inspiration, at the height of which the liver-puncture needle is inserted quickly as far as the abdominal cavity and the stylet is removed. The patient next makes a deep expiration and holds his breath. At this moment, to avoid squeezing or tearing of the liver tissue, the needle is quickly pushed in up to the regulator, attached to a 20 ml. syringe, and twisted to and fro around its axis while the assistant aspirates liver tissue. The inner needle with the syringe is then removed and the citostat solution is injected through the outer needle. The whole operation lasts only a few seconds. The site of puncture is covered with a piece of sterile gauze kept in place with adhesive plaster. The patient is immediately given an injection of morphine and atropine and taken to his bed on a stretcher. There he has to lie still for 24 hours with an ice-bag at the site of the puncture. He should not eat or drink within 3 hours after the puncture.

The aspirated piece of liver, about 2–3 cm. long and 2 mm. thick, is either in the syringe or in the lumen of the inner needle. In the latter case fixing fluid is passed through the needle. The fixing fluid is 10% formalin or absolute alcohol if glycogen stain is to be applied, or, if inclusion bodies are to be stained, Dubosq-Brazil-Born's solution (picronitric acid 1 part, 80% alcohol 150 parts, 40% formalin 60 parts, pure acetic acid 15 parts).

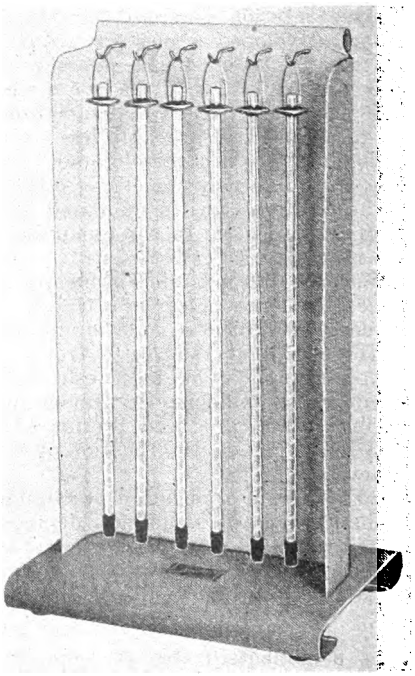
Some patients feel a slight pain at the site of the puncture or in the right side, and rarely in the shoulder as a sign of injury to the diaphragm. The pain does not last longer than 24 hours. In some cases there is slight pyrexia for 24 hours; in only 2 cases out of 65 did pyrexia last for some days. No sign of hæmorrhage was observed. The citostat forms a firm thrombus, as was seen at necropsy of a patient with cancer who died a week after liver puncture. The site of the puncture was still visible with a firm and partly organised thrombus in its centre (fig. 2).

Apart from the effect of the thrombin solution, we ascribe the freedom from complications in our cases * to the use of a needle which will not pass deeper than 3 cm. into the liver.

New Inventions

MODIFIED STAND FOR SEDIMENTATION TUBES

THE stand illustrated here was designed by Mr. J. R. Hancock, senior technician in the department of physiology at St. Mary's Hospital medical school, for avoiding large errors in measurement caused by sedimentation tubes not being vertical (particularly when the sedimentation-rate is high). The tubes are hung in special holders which ensure that the point of suspension is strictly in alignment with their axes.



The Wintrobe tubes are filled in the ordinary way. Westergren tubes are first sealed with a rubber cap at the lower end, and then the blood is injected through the cap into the tube from a syringe fitted with a fine hypodermic needle. Experiments show that the rubber cap will stand many such punctures before it starts to leak. The rubber cap has another important function—by moving it on or off the level of the blood can be accurately adjusted to the zero mark.

Tests have shown that pendulum movement through a 1 in. arc is without effect on the sedimentation-rate, though such movements far exceed those produced by draughts or vibration in normal practice. Estimations done by an open window showed that an ordinary draught did not produce sufficient continuous displacement to alter the result.

These stands can be obtained from Messrs. A. Gallenkamp & Co. Ltd., 17–19, Sun Street, London, E.C.2.

A. ST. G. HUGGETT, M.B., D.SC., PH.D. Lond.
Professor of Physiology, University of London.
St. Mary's Hospital Medical School, London.

* By Feb. 14, 1949, we had used this technique in 200 cases, and no untoward symptoms had been observed.

Digitized by Google

Reviews of Books

Trace Elements in Food

G. W. MONIER-WILLIAMS, O.B.E., M.C., M.A. Oxfd, PH.D Freiburg, F.R.I.C., formerly inspector of foods, Local Government Board, and chemist in charge of food research laboratory, Ministry of Health. London: Chapman & Hall. 1949. Pp. 511. 30*s*.

OF those qualified to write a book on this subject, few could have written one so interesting, practical, and concise.

Twenty-nine elements are discussed: copper, lead, zinc, tin, arsenic, antimony, selenium, iron, nickel, cobalt, manganese, iodine, bromine, fluorine, boron, silicon, aluminium, silver, cadmium, chromium, bismuth, mercury, molybdenum, vanadium, titanium, indium, barium, strontium, and lithium. Thus the book covers both the physiological and the toxic elements, and also those—such as aluminium, silver, and strontium—which are not of much practical importance but which for one reason or another come within the purview of the public analyst. Each chapter opens with a section on the physiology or toxicology of the element, including as a rule an account of its absorption and excretion. The amounts in food are usually given and the reasons why the element comes to be present in the foods. Then follows a survey of the methods of assay, and each chapter closes with a bibliography.

There are a few small omissions. The bizarre amounts of some of the trace elements which have been found in some of the marine invertebrates might have had more attention. The methods given are predominantly chemical; though spectrographic methods of analysing some of the elements (e.g., cobalt), are mentioned, the reader may not realise what a help these methods have been in developing the subject. It is bad luck that the association of cobalt with the anti-pernicious-anæmia factor was discovered just too late to receive a mention. But these are minor suggestions, possibly for the second edition. The book should be of great service to analysts and physiologists, and useful to many other people whose interests are less specialised.

Techniques in Physiotherapy

Editor: F. L. GREENHILL, S.R.N., M.C.S.P., sister-in-charge, medical rehabilitation unit, Royal Free Hospital; assisted by C. B. HEALD, M.D., F.R.C.P.; J. N. BARRON, F.R.C.S.; J. COLSON, M.C.S.P., M.A.O.T. London: Hodder & Stoughton. 1948. Pp. 222. 12*s*. 6*d*.

IN its classifications of rheumatism—one ætiological, the other anatomical—this book is unorthodox; and it contains many statements with which one may or may not agree. Histamine-ionisation and short-wave diathermy are recommended for menopausal arthritis; "concentration on the rehabilitation of the skin function" is described as the key to success in the treatment of gout; in all rheumatic conditions "elimination by the liver and the bowel" is held to be most important; and colonic lavage and faradic stimulation of the abdomen and back are advocated as assisting in the better function of the bowel. The description of rheumatoid arthritis is brief but generally acceptable, though it is puzzling to find "infective arthritis" described as a separate entity. The section on osteo-arthritis deals almost entirely with the hip, and largely with operative procedures; while outdated orthopædic manœuvres are described, the treatment by 'Vitallium'-mould arthroplasty, and the physiotherapeutic techniques required after operation, are not mentioned. The chapters on physiotherapy "in some nerve conditions" are helpful; and the electromyograph and interpretations of its findings are included. Also there are good chapters on the treatment of chest conditions and burns and injuries. Miss Greenhill is very much at home on exercises and similar treatments, and her description of group exercises is excellent. In dealing with exercises for abdominal conditions she gives an account of the various abdominal incisions which physiotherapists will find valuable. The suspension exercises which have come to play so large a part in physiotherapy are well described and illustrated, and occupational therapy gets a useful chapter. A final chapter on the relations between the doctor and the physiotherapist reflects the present attitude of the medical profession to physiotherapy: with some justification, Miss Greenhill feels obliged to explain the subject simply to the doctor in order that he may take his rightful place in its prescription. Her book is evidently intended both for doctors and physiotherapists, and it is clearly illustrated with diagrams and photographs.

Occupational Therapy Source Book

Editor: SIDNEY LICHT, M.D. Baltimore: Williams & Wilkins. 1948. Pp. 90. $1.

STUDENTS who have so little time to do so many things in will find it easy to skim through this short book dealing with the history of humane treatment of the mentally afflicted. They will gain from knowing something of the aspirations, common sense, and noble work of their forerunners. A lively paper on the history of occupational therapy, by the editor, starts the book. This is illustrated by well-chosen quotations. Then follows a series of excerpts and separate chapters taken from the works of Pinel, Rush, Tuke, Leuret, Kirkbride, and others, and each is prefaced by a short biographical note. For antiquarian pleasure there are two reproductions of original title pages. An English reader will find it especially refreshing to be led to unknown American sources. Dr. Jarvis in the *American Journal of Insanity* for 1862 gave a thoroughly neat description of the aims and value of occupational therapy.

Joseph Lister: the Friend of Man

HECTOR CHARLES CAMERON. London: Heinemann Medical Books. 1948. Pp. 176. 17*s*. 6*d*.

Dr. Charles Cameron brings a sympathetic understanding to bear on this intimate study of Lord Lister. He is indebted to his father, Sir Hector Cameron, for much of his insight into Lister's personality and work, but his own appreciation informs the book. Lister, Pasteur, and Koch were a great triumvirate of the 19th century; and Lister was great as a man even before he became great as a surgeon. Shy and diffident, he shrank from controversy and suffered much from the ill-natured opposition and ridicule of some of the leading men in his own profession. But he did not deviate from the course he had set himself; and, though the prophet was at first without honour in his own country, his methods spread rapidly on the Continent. With Pasteur—to whom he freely acknowledged his debt—his relations were happy. Describing Lister's daily life, and the devotion of his wife, Dr. Cameron tells the simple story of a man of high principles and high achievement.

Radio-active Indicators

Their Application in Biochemistry, Animal Physiology, and Pathology. GEORGE HEVESY, Institute for Research in Organic Chemistry, University of Stockholm, and the Institute for Theoretical Physics, University of Copenhagen. New York and London: Interscience Publishers. 1948. Pp. 556. 60*s*.

ALTHOUGH written by a Scandinavian, this is a typical American "review" volume. It is packed with miscellaneous and up-to-date information on the subject, but is quite unreadable and nowhere provides an over-all estimate of the relative value of the information gained by the use of radioactive indicators. It is a book for the "dipper" or for the reference library shelf. If you want to know whether radioactive indicators have been applied to this or that problem, or to what uses radio-X has been put, the excellent index provided will lead you smartly to the information, accompanied by references for further detail.

This sort of information takes up the bulk of the volume and it is agreeably factual: the biochemist will find details of the applications of C^{14} and triterium; the hæmatologist will find a review of the application of radio-iron to iron metabolism problems and he can learn that the radio-phosphorus in thromboplastin is not carried over into the thrombin; the dentist will find a discussion of the deposition of radiophosphorus in dentine and enamel; and so on. There are also some highly technical sections on the preparation of

Digitized by Google

radio-isotopes and the estimation of their activity. In a pocket on the back cover is a " Segré chart "—a remarkable affair looking like a nightmare crossword puzzle—that tells you, if you can read it, the characteristics of all known isotopes. Lists of available isotopes, their characteristics and sometimes their price, are given.

The book certainly does what it sets out to do; but, as the author points out, there is no future for this type of survey, because the results obtained with radioactive indicators will be incorporated into descriptions of specific subjects. We agree: in a book of this type so much appeals—and in fact is only intelligible to—workers in special fields.

Principles of Biological Assay

C. W. EMMENS, D.SC., PH.D., National Institute for Medical Research, London. London: Chapman & Hall. 1948. Pp. 206. 21*s*.

MOST workers on biological assay recognise the inaccuracy of their tests and have learnt how to estimate the inaccuracy of each particular test, or of a series of tests, in ways which were scarcely dreamed of twenty years ago. This they have done by studying general principles of statistical method, and by discussing their problems with mathematicians. The mathematicians became interested in biological assay, and the methods they developed for estimating the accuracy of tests are gradually being accepted and applied. The book under review is the outcome of that growing interest. It will be of great value to workers concerned with biological assay, whether the assay involves a response graded to the dose of test substance or a response known as an " all or none " reaction. Dr. Emmens has obviously given thought not only to the actual assays, of both these kinds, which have come his way, but to the principles pervading this kind of work. His book should incidentally help towards a greater uniformity of notation which would simplify matters for both younger and older students of statistical method.

Pathologie des Kohlehydratstoffwechsels

E. FRANK, director of the II medical clinic, University of Istanbul. Basle: Schwabe. 1949. Pp. 342. Sw. fr. 24.

Professor Frank opens with a historical survey of the subject, which he divides into the usual stages, and concludes with a section on alloxan diabetes. When reviewing the work which culminated in the discovery of insulin he points out that it was perhaps a matter of chance that this took place in North America, but he adds that the rapid development, production, and standardisation of insulin there was a characteristically American effort. He then deals with the clinical aspects of pituitary diabetes before passing on to discuss insulin, to which he devotes a chapter. He discusses the pathological anatomy of the pancreatic gland in diabetes and the effects of carcinoma and acute necrosis on the islet tissue, and then goes on to the functional and chemical pathology of the disease. There are chapters on diabetic acidosis, diabetic coma and its treatment, and hypoglycæmia—or, as the author prefers to call it, hyperinsulinism. The last 80 pages of the book are devoted to chapters on the " glycogen " disease, the association of aneurin with carbohydrate metabolism, renal thresholds, and rarities such as pentosuria and fructosuria. It will be seen from this synopsis that the book has been planned and written on conventional lines and that clinical interest is well to the fore. It does not offer the last word on carbohydrate metabolism, but the historical touches are good and the general information sound. The treatment of the references is perhaps the weakest part of the book. Many authors are quoted by name in italics throughout the text, yet their names do not appear in the rather attenuated and unalphabetical list of references at the end. With these reservations the book may be recommended to advanced students who can read German, and it will be found very useful by anyone who wishes to prepare a lecture on the subject. It is not really a work for the general practitioner, and its value to students and lecturers lies in its balance and approach, which must be instructive to anyone versed only in the English and American literature.

Péan (Paris: Maloine. 1948. Pp. 242.).—Dr. Robert Didier gives a faithful account of the life and work of a remarkable man. Péan was of peasant stock, rugged physical strength, and strong personality. According to Dr. Didier he may be classed among the great surgeons of France and indeed in the succession of Dupuytren. In his earlier career Péan was fortunate enough to be a pupil of the great Nélaton. But he was an original genius and rose to fame chiefly by his work in abdominal surgery and his development of the artery forceps in the control of hæmorrhage. Perhaps he is known best by the introduction of vaginal hysterectomy, which he brought to a fine art, thus avoiding the risk of peritoneal complications.

Cunningham's Manual of Practical Anatomy (11th ed. London: Oxford University Press. 1948. Pp. 387. 21*s*.).—This old friend, like a stout dowager after a month on orange juice only, is now slender and elegant. However, like a good corsetière, Prof. J. C. Brash has achieved his purpose less by reduction and compression than by a better distribution of the mass. Detail remains; for, as he says, a manual too closely shorn of detail is likely to inculcate a habit of superficial observation. He believes that descriptive detail which is not of immediate, or even perhaps of ultimate, value to the doctor, is yet an element in scenic description, helping the student to learn his way about the body just as he would learn his way about a new district. Nevertheless he has saved a good deal of paper, and probably a corresponding proportion of his readers' time. We hope that in the next edition the dark old over-lettered pictures will be replaced by others more appropriate to the contemporary text.

Practical Public Health Problems (2nd ed. London: J. & A. Churchill. 1948. Pp. 197. 14*s*.).—The great changes in public-health practice brought about by the National Health Service Act, 1946, do not affect the problems with which Sir William Savage dealt in his first edition; so no drastic revision of the text was necessary. But the second edition contains two new chapters—on the investigation of enteric outbreaks, and on dealing with an outbreak of infectious diseases. The chapter on the Food and Drugs Act, 1938, has been replaced by one on hygienic food control. This book is a successful attempt to convey to beginners the experience of a great master of the art of using what has been learned. When it was written in 1941, public-health practice was overloaded with duties out of the direct line of communal hygiene, which had become a somewhat " neglected terrain " by medical officers; but the Act of 1946 has brought back this ground as the main field of their activities. This will increase the popularity of this serviceable volume. It is not a textbook, but a series of personal talks, in which Sir William walks companionably beside his younger colleagues in their routine duties; and very thankful they will be to have such a wise practitioner at their elbow.

Psychobiology and Psychiatry (2nd ed. London: Henry Kimpton. 1948. Pp. 620. 45*s*.).—This book by Dr. Wendell Muncie is avowedly a monument to Adolf Meyer. It would therefore be reckoned a failure if it did not, in expounding his teaching, convey to the reader something of the impression he left on his pupils, and make it understandable that he became the undisputed leader of American psychiatry—and to a considerable extent a dominant influence in English psychiatry too—for a quarter of a century. In this sense the book is a partial success: but it cannot recapture the example he constantly afforded those working in his clinic of how to combine exactitude with a capacity for comprehensive synthesis; he showed how tolerance and humane regard must join with critical judgment, whether one was examining the history of the individual patient and treating him, or trying to solve some scientific problem. It is a merit in the book that, faithful to Adolf Meyer's conception of psychiatry, it has nothing to offer those who want a short textbook that they can memorise and use for examination-answering. It is studded with detailed case-histories and comments on them, and contains no dogma about psychopathology or methods of treatment, whether physical or psychological. It succeeds in presenting not so much the facts of psychiatry as the habitual point of view, which should become second nature to the psychiatrist in all his clinical activities, since without it he falls victim to extremism or windy speculation.

Digitized by Google

THE LANCET

LONDON: SATURDAY, MARCH 26, 1949

Further Thoughts on Specialist Salaries

PAST deficiencies in our specialist services have been caused partly by a scarcity of fully trained specialists, and partly by their uneven distribution. Obviously then, if we are to have the comprehensive service now promised, we must attract more recruits to the specialties, and arrange that eventually they are so domiciled as to serve all parts of the country. The first object may be well within our grasp. Even as they stand today, the proposed terms of service should suffice to attract all the trainee specialists that may be needed. Indeed, as the *Times* pointed out on March 17, the chief danger lies in their being so much more generous than those offered to the general practitioner; for they may thus defeat one of the aims of the original Spens report—namely, that the rewards of general practice should compare well enough with those of other professions, and other branches of our own profession, to ensure that able men and women will continue to work as general practitioners. The proposals published last week seem to load the balance heavily in favour of specialism. No longer will the newcomer have to serve his specialist apprenticeship virtually unpaid, as he so often did in the past. He will hold a succession of increasingly responsible and adequately paid trainee appointments until he is recognised as of full specialist status; after which he can look to a secure and rising income, with a very fair chance of a merit award in the fullness of time. Even should he be among those who fail to achieve recognition as full specialists, he may yet find a niche for himself in the grade of senior hospital medical officer, which still offers a net income greater than that achieved, on the average, in general practice. His holidays are secured, sickness is provided for, and paid study leave encouraged, by the provision of a locum tenens; whereas the general practitioner must provide his own substitute at his own expense. The superannuation arrangements also favour the specialist. While the general practitioner is pensioned on a proportion of his average earnings throughout his years of service, the specialist's pension will be based on his average remuneration during his last three years, including any merit award he receives. Incidentally the fact that merit awards are superannuable makes it probable that they will be given early rather than late in the recipient's career:

Fixed percentages of specialists (4, 10, 20) are to receive awards in the three grades; and the number thus distinguished can be found by multiplying these percentages by a factor determined by dividing the average length of a specialist's active life (say 30–35 years) by the average number of years during which he may expect to enjoy a merit award. If awards are given late, and consequently held for only a short time more specialists will reach the higher incomes and retire on the larger pensions, and each individual will have contributed less to his superannuation. Actuarially therefore the advantage will lie in distributing the awards as early as possible.

But at whatever age the steps in income are achieved, it is clear that the reasonably successful specialist is likely to retire with a much better pension than his colleague in general practice.

All these factors tend to make general practice less and less attractive, and together they reinforce the case for improving immediately the general practitioner's remuneration in the new service. It is true that claims are already being put forward for granting more money to general practitioners; but these are based mainly on the plea that, in determining the total sum payable to them, too little attention has been paid to changed money values, and insufficient betterment has been granted. The same argument will be advanced by the specialists, some of whom also seem intent on claiming a higher betterment factor. It should be recognised, however, that if both claims were granted, in equal proportion, the effect would be to widen yet further the gap between the remuneration of these two sections of the profession. It would be safer for the general practitioners to base their claim on deserving to enjoy an income that would compare not too unfavourably with that eventually awarded to their specialist colleagues.

Then there is the question of distribution. It might be thought that by creating extra posts for specialists in all hospital management areas, and by paying these posts equally wherever established, the regional boards will automatically solve this problem. Unfortunately, however, the solution is not so simple as that. The best-paid consultants will be those who are able to undertake a liberal number of part-time sessions and combine them with private practice, teaching, and a merit award. Opportunities for private practice, for teaching, and for the ubiquity which many specialists will think necessary to recognition, is likely to exert a centripetal force, leaving the remoter areas still under-provided with full specialists. These areas may then find themselves obliged to employ a high proportion of senior hospital medical officers to carry out in hospital the duties elsewhere performed by more senior specialists. The proposed terms of service give no indication that in such circumstances these senior hospital officers would also be available for domiciliary consultations; and if they are not available the whole system of domiciliary consultation may break down in some parts of the country. General practitioners are already finding consultants reluctant to travel far from their agreed centre for domiciliary visits within the service, and the time and mileage payments now suggested are unlikely to overcome this reluctance.

Finally, what about the general practitioner who now does specialist work for part of his time? His future position is far from clear. It seems certain that, in granting permanent contracts to a general practitioner for specialist services, regional boards will have to satisfy themselves that he is not attempting so much sessional work that neither side of his professional duties can be satisfactorily performed. Often this may mean that any doctor who is still in general practice will find his specialist contract limited to the equivalent of two or three (or at most

Digitized by Google

four) weekly sessions. Should he also find that the reviewing board has felt unable to recognise his work as of full specialist standard, he may well conclude that the reward he is offered, as a limited part-time senior hospital medical officer, does not justify the time and trouble, and the reorganisation of his general practice that is so often involved. He may then be driven to choose between giving up his part-time specialty or his general practice; and sometimes the area he has served in his dual capacity will lose rather than gain by the change.

Radio-iodine in Thyrotoxicosis

THE thyroid's enormous capacity for concentrating iodine gives the physiologist an almost unique opportunity of applying the tracer technique to an organ at work. For the most part work done with radio-iodine since 1938, when it was first available for research, has confirmed, in a more elegant and precise manner, what was already known or at least surmised. Sceptics may maintain that no truly original discovery has yet been made by the use of radio-iodine, but the substitution of firm facts for what was sometimes little more than guesswork is undoubtedly a valuable advance. A good example is the work done by LEBLOND and GROSS,[1] of McGill University, on radio-autography of the thyroid. Histological sections of rat's thyroid were prepared in the normal manner, after a preliminary dose of radio-iodine. The sections were stained and then coated with a photographic emulsion, sensitive to the rays emitted by radioactive material. The resulting picture as seen under the microscope enables the observer to study the location of the iodine atoms against the normal histological background. These studies do not reveal anything not previously suspected, but they provide information about the detailed workings of the gland which is much fuller than any that could be obtained by the classical methods of cytology.

It would be easy to add examples of this sort from the expanding field of thyroid physiology, but the clinician is more interested to know what radio-iodine has to offer in the way of improved diagnosis and treatment, particularly in thyrotoxicosis. The diagnosis of the florid case of toxic goitre is always easy. Such cases make up a considerable proportion of the whole, but there remains a wide fringe of doubtful cases. In some of these estimation (with proper precautions) of the basal metabolic rate is very helpful, but long experience of this test shows that it is not infallible. When doubt remains, use may be made of a diagnostic course of iodine, or of one of the thiouracil drugs. The latter usually give a more clear-cut response, and have no effect on subjects with normally functioning thyroids within about a month.

Though these tests usually enable the experienced clinician to come to a correct decision, he would welcome extra help and would gladly be freed from the defeatist manœuvre of the therapeutic trial. The claims of radio-iodine must therefore be carefully examined. The two diagnostic methods in common use were both originated by HAMILTON and SOLEY,[2] of the University of California. These workers gave a small dose of radio-iodine and then estimated the amount put out in the urine after different intervals. Their normal subjects excreted rather more than half the dose within 24 hours. One untreated thyrotoxic patient excreted much less; and it was assumed that the excess was retained by the thyroid. In the second method, the emission of gamma rays by the thyroid was directly measured by placing a Geiger counter in front of the subject's neck. After a test dose of radio-iodine the radioactivity in the neck region increased more rapidly, and reached a higher level, in thyrotoxic than in normal subjects. Many workers have confirmed and extended these findings.[3] Certainly thyrotoxic patients excrete a smaller proportion of the radio-iodine, and most of the remainder is located in the thyroid. But the more the subject is studied the more apparent does it become that the separation of normal and thyrotoxic subjects by these two methods is not absolute. In a symposium on radio-iodine held in New York HERTZ[3] described both methods as "disappointing."

More recently a third method has been developed in this country by POCHIN[4] and his colleagues. This is rather more elaborate, but the separation of the normal from the thyrotoxic seems to be sharper. Briefly, the method consists in simultaneous estimation of the rate at which radio-iodide is entering the thyroid, and of its concentration in the plasma. The former is estimated by observing the rate at which gamma rays are being emitted from the neck, and the latter by the beta-radiation of a sample of plasma. Knowing the percentage of the dose taken up each minute by the thyroid, and the corresponding percentage in a given volume of plasma, it is possible to estimate the volume of plasma which is being cleared of iodide each minute. The "thyroid clearance rate" thus obtained is interpreted in a similar sense to the more familiar renal clearance. The normal subject clears about 16 ml. of plasma per minute into his thyroid, whereas the thyrotoxic subject clears over 100 ml. per minute. Theoretically the difference between the clearance rates of normal and thyrotoxic subjects is likely to be considerably greater than the corresponding differences between urinary excretion rates or simple thyroid uptake rates; and this seems to have been confirmed in practice by POCHIN. The technique is therefore likely to become a standard method of demonstrating the characteristic avidity of the thyrotoxic thyroid for iodide. This biochemical abnormality is only one aspect of the disease, but so far it appears to be quite closely related to the output of hormone by the gland; and it is the greatly increased output of hormone which causes the major part of the clinical syndrome. The test will be invaluable to research-workers; but, the technique being elaborate, it is unlikely ever to come into general use.

The fact that radioactive iodine can be introduced in much higher concentration into the thyroid than into the other tissues of the body—particularly in toxic goitre—invites trial of its therapeutic effect. The attempt was first made by HAMILTON and LAWRENCE[5] and HERTZ and ROBERTS[6] in 1942; and

1. Leblond, C. P., Gross, J. *Endocrinology*, 1948, **43**, 306.
2. Hamilton, J. G., Soley, M. H. *Amer. J. Physiol.* 1939, **127**, 557; *Ibid*, 1940, **131**, 135.
3. Brockhaven Conference Report: Symposium on Radio-iodine. 1948.
4. Myant, N. K., Pochin, E. E., Goldie, E. A. *Quart. J. Med.* 1948, **17**, 329.
5. Hamilton, J. G., Lawrence, J. H. *J. clin. Invest.* 1942, **21**, 624.
6. Hertz, S., Roberts, A. *Ibid*, p. 624.

Digitized by Google

the results of six years' experience were described by three speakers at the New York symposium. There was general agreement that thyrotoxicosis can be adequately controlled whether the radio-iodine is given in a single large dose or in repeated small ones. From the patient's point of view the method is admirably simple: he drinks a glass of water and his treatment is completed; and the effect seems comparable to that of subtotal thyroidectomy or to treatment with an antithyroid drug. Nevertheless certain anxieties have so far prevented the general adoption of this method. First, it is difficult to judge the dose required, because no method exists for measuring the size of the intact human thyroid; hence myxœdema may sometimes ensue. This danger is best averted by giving all patients a preliminary tracer dose of radio-iodine; the rate of uptake by the thyroid can then be assessed before treatment is started. The second, and less prominent, fear is that the radioactive material will initiate in the thyroid or possibly the urinary tract (the two sites in which it is most highly concentrated) changes leading eventually to cancer. So far no such changes have been reported; but cases will have to be observed for some twenty years before the possibility is excluded. The third fear is of harm to the sex organs, conceivably with genetic changes revealed only in the offspring. This risk must be exceedingly slight, but it will be much more than twenty years before the bogy can be finally laid. Meanwhile this therapy might reasonably be reserved for patients above the menopausal age.

If radio-iodine were the only agent to control thyrotoxicosis, the benefit to the patient would outweigh both the technical difficulties and the relatively slight dangers. But it is not; both subtotal thyroidectomy and the antithyroid drugs enable us to control this disease quite effectively. Recurrence after thyroidectomy is, however, often rather difficult to treat by the usual methods; a second operation entails increased risk to the parathyroids and recurrent nerves, while thiouracil seldom provides lasting remission. Here the use of radio-iodine might be justified in postmenopausal subjects. With this possible exception, clinicians in this country will probably prefer their patients to be exposed to the known drawbacks of the well-tried methods, rather than to the potential hazards of radioactive material.

Health Insurance in America

THE unexpected election of Mr. TRUMAN as President of the United States has encouraged the American supporters of compulsory health insurance. He has long been keenly interested in measures for the promotion of the health of the American people; and the approval he gave to the report addressed to him last September [1] by Mr. OSCAR R. EWING, Federal Security Administrator, showed that he was in favour of the enactment of compulsory health insurance. The advocates of this measure, in the legislature and elsewhere, are hopeful and active.

Its opponents are equally active. Foremost among them is the American Medical Association, which for many years has consistently opposed compulsory health insurance, holding it to be an instalment of "socialised medicine," which would bring the medical profession under bureaucratic control, impair the doctor-patient relation, and by lowering the standards of medical practice, ethical and technical, inflict irreparable damage upon the health of the nation. In England compulsory insurance has led to the National Health Service, which, according to the *Journal of the American Medical Association*, has displayed "the utter inability of the doctors, the hospitals, the pharmacists, and the dentists to meet the demands made upon them." Dr. MORRIS FISHBEIN, editor of the *Journal*, writes in the issue of Dec. 25, 1948:

> "My personal observations in England led me to the opinion that the quality of medical service rendered under the National Health Act would never be satisfactory to the average American laborer or farmer. The greatest mistake that England made in adopting its National Health Act was its failure to realise that even moderately good functioning of such an act depends on adequate medical personnel and medical facilities. These England did not have. British politicians felt that any kind of medical care was better than no medical care. That is a hazardous hypothesis."

The association has decided to make an assessment of 25 dollars per member for the purpose of creating a fund "to educate the American people as to the nature of medical practice in the United States." It holds that they should know "that compulsory sickness insurance is not a technic for providing free medical care to all of the people but instead a system whereby the workers of the nation are taxed to support a vast bureaucracy which itself will distribute medical care and which will be the intervening agency between the sick and the medical, hospital, pharmaceutical, nursing and allied professions." Since the association has 135,000 members, the sum accruing from the assessment should be large; and a large sum will be necessary, for the educational campaign contemplated by the association is one that "will reach the very grass roots of the nation." When this educational project became known, the headquarters of the association were besieged by hundreds of advertising agencies, motion-picture producers, experts in propaganda, and the like, eager to participate. It was decided, however, to entrust the formulation of a plan to a Californian firm as "special public relations counsel." The policy of the association is to present to the public not only a destructive case against compulsory health insurance, but a constructive system of measures for improving the nation's health, and, in particular, for providing adequate medical care for persons unable to pay for it as ordinary private patients. A twelve-point programme appearing in the *Journal* for Feb. 19 recommends a wide extension of voluntary insurance against the costs of hospital and medical care, with aid through the States to indigent and "medically indigent" persons. Funds would be administered in each State by a "medical care authority" with "proper representation of medical and consumer interest." It is also recommended that a Federal department of health should be constituted with a medical head, who would have Cabinet status; that public funds should be made available in aid of research and the training of doctors, dentists, and nurses; and that extended provision should be made for preventive medicine, mental health,

1. The Nation's Health. See *Lancet*, 1948, ii, 574.

Digitized by Google

and the care of old persons. The association points out that in the U.S.A. voluntary health insurance has during recent years made remarkable progress in popular favour. In 1947 the persons voluntarily insured against hospital costs numbered 44 million. Between 1944 and 1947 the number of persons insured under private group health-insurance schemes rose from 7 million to 14 million. There are 70 schemes of voluntary health insurance in operation under the management of the local doctors. The association contends that voluntary methods of prepayment practice are better suited to American conditions than bureaucratic governmental methods would be.

Some critics of the association's former policy concerning "socialised medicine" regard these new proposals as marking a considerable advance towards acceptance of the principle of governmental intervention to secure adequate medical care for persons described as "medically indigent." This last is an elastic term, susceptible of more than one interpretation—capable, indeed, of acting as the thin end of a wedge. The association's critics point out also that its reliance on voluntary insurance to bring medical care to the mass of the people has been shown by experience to be without adequate foundation. In countries where voluntary health insurance was most widely adopted, it was found that it did not provide for many of those who were most in need of it—those who, though not indigent, were, or thought they were, too poor to pay regular insurance contributions. Extensive development of voluntary health insurance has generally led to the adoption, sooner or later, of compulsory health insurance.

To some observers of the American scene at the present time the need for health insurance seems less pressing than in the early 1930s, the time of the great economic depression. The country is prosperous; the general standard of living is higher perhaps than at any former time; and there are now many more people able to pay their doctors' bills than there were in 1932, when the report of the Committee on the Costs of Medical Care appeared. Nevertheless Mr. TRUMAN has asked Congress to consider legislation for expanding old-age and unemployment insurance, and though he has not yet taken similar action in regard to compulsory health insurance—a much more controversial subject—this seems likely soon to become a live issue in the legislature and in the country.

Annotations

MARROW BIOPSY

THE hazards of sternal puncture, to which we referred last year,[1] have been investigated by Rubinstein,[2] who concludes that fatalities are much commoner than the literature might suggest. He therefore advocates the alternative method of aspirating bone-marrow from the iliac crest.

This procedure is not new. Nordenson,[3] for instance, mentions that in 2 normal subjects he obtained marrow by aspiration of the manubrium sterni, a rib, each iliac crest, and the body of the third lumbar vertebra; he found surprisingly close agreement between the different samples. Van den Berghe and Blitstein [4] compared differential counts of iliac and sternal marrow samples in 2 normal subjects, and in a patient with secondary anæmia and another with myeloid leukæmia; again agreement was close. They favour iliac-crest puncture, less because of the risks attending sternal puncture (which they believe to have been exaggerated) than because patients are apprehensive when a needle is employed near the heart; their patients preferred iliac puncture. This is generally a less painful operation; and, they assert, it can be carried out with safety on small children. Rubinstein claims further advantages for this method, which he has practised more than a thousand times. To the operator it is a relief to know that, with the needle directed downwards from the iliac crest towards the lower extremity, there is no danger of penetrating an inner plate; moreover, for serial examinations the two crests offer a choice of site. Rubinstein made parallel studies on sternal and iliac marrow in 216 patients. In those with normal findings (their ages ranged from 16 to 78) the iliac crest always provided hæmatopoietically active marrow; and the cell distribution showed approximately the same range as sternal marrow. In general this parallelism existed also in pathological marrows, but iliac aspiration yielded fuller information than sternal marrow in four groups. Firstly, in 3 patients whose sternal marrow had repeatedly proved hypocellular, iliac puncture revealed the classical cytology of leukæmia, which was later discovered also in the sternal marrow. Secondly, in 3 cases of multiple myeloma where sternal puncture was inconclusive, the diagnosis was indicated by iliac-marrow films; and in 2 of these with thrombocytopenia and a bleeding tendency, the material obtained by sternal puncture was too diluted with blood to be of real use. Thirdly, in some instances of aplastic anæmia and osteosclerotic anæmia sternal puncture revealed an aplastic bone-marrow, while by iliac aspiration islands of active hæmopoietic tissue were found; in other cases, however, the reverse held. Finally neoplastic cells were found more commonly in marrow from the ilium than from the sternum.

With research-workers the ilium is already a favourite source of marrow,[5] and the method described by Rubinstein will probably be increasingly popular with clinicians. A further method, by which marrow is aspirated from the spinous processes of the vertebræ, was described in 1936 by Heidenreich and Heidenreich,[6] and has been used with success by de Weerdt.[7] All these three workers seem, however, to have found sternal puncture easier, and de Weerdt believed that the sternal method is more likely to yield active marrow. Nevertheless, this technique has lately been revived and advocated by Loge.[8] In 25 patients, all in hospital with upper-respiratory infections, samples of marrow from spinous processes and from the sternum were found to be remarkably similar; and it is noteworthy that in 2 elderly patients, aged 75 and 72, the cellularity of the vertebral marrow was equal to that from the sternum. When questioned, 13 of the patients said that they preferred the vertebral approach and 7 the sternal method; 5 expressed no preference. Loge, though not suggesting that the sternal technique should be discarded, points to the value of an alternative approach, especially in young children, where the risks of sternal puncture are greater than in adults.

One method of marrow biopsy may succeed where others fail [9]; and hæmatologists are likely to make increasing use of the alternatives to sternal puncture.

1. *Lancet*, 1948, i, 566.
2. Rubinstein, M. A. *J. Amer. med. Ass.* 1948, **137**, 1281.
3. Nordenson, N. G. Studies on Bone Marrow from Sternal Puncture. Stockholm, 1935.
4. Van den Berghe, L. P., Blitstein, I. *Pr. méd.* 1945, **53**, 419.
5. Ho, E. A., Chu, H. J., Yuan, I. C. *Chin. med. J.* 1940, **58**, 679. Meyer, L. M., Bloom, F. *Amer. J. med. Sci.* 1943, **206**, 637. Sawitsky, A., Meyer, L. M. *J. Lab. clin. Med.* 1947, **32**, 70.
6. Heidenreich, A. J., Heidenreich, G. L. *Prensa méd. argent.* 1936, **23**, 2818.
7. de Weerdt, W. *Rev. Belge Sci. méd.* 1939, ii, 297.
8. Loge, J. P. *Blood*, 1948, **3**, 198.
9. Dameshek, W. *Ibid*, p. 209. Dacie, J. V., White, J. C. *J. clin. Path.* 1949, **2**, 1.

Digitized by Google

AMYLOIDOSIS IN RHEUMATOID ARTHRITIS

AMYLOID disease is a recognised sequel to chronic phthisis, chronic osteomyelitis, and syphilis; occasionally it is found with lymphadenoma and myelomatosis; and more rarely a so-called "primary" or localised form affects the skin, tongue, œsophagus, lung, heart, or pericardium, or even the thyroid where amyloid is deposited either diffusely or as a tumour mass. In animals amyloidosis is seen in horses used for making diphtheria antitoxin, and in small rodents it can be produced experimentally by parenteral injection of a caseinate, nutrose, and (in mice) by feeding with cheese [1]; it also occurs with infection by pyogenic organisms and in tuberculous and tumour-bearing animals. The course of the illness is nearly always slowly progressive to a fatal issue, though both in man and animals resorption may follow prompt removal of an infective focus—as, for example, by amputation of a limb for osteomyelitis.

The association of amyloidosis with Still's disease in children and with rheumatoid arthritis in adults was first described by Whitman and by Spitzy, in 1903. Records of rheumatoid arthritis thus complicated now number between 30 and 40; most are in the American literature, but in the last two years several instances have been reported in this country.[2,3] In two cases recovery from the amyloid moiety is reported to have followed intensive liver therapy.

Of these two cases, the first, recorded by Trasoff, Schneeberg, and Scarf,[4] of Mount Sinai Hospital, was in a 14-year-old girl with severe multiple rheumatoid arthritis (Still's disease), who within four months of onset showed splenomegaly, hepatomegaly, albuminuria, and anæmia, together with puffiness of the face, hypoproteinæmia, and inversion of the albumin/globulin ratio; this suggested renal amyloidosis, which was later confirmed by repeated congo-red tests. In treatment high-protein diet and plasma infusions proved ineffective. Then, in the light of promising experimental results,[5] liver extract was injected for many months. This brought about gradual improvement with diminution of peripheral œdema and of massive pleural effusions and ascites; but hypoproteinæmia with relative hyperglobulinæmia persisted. Nevertheless within the year œdema and joint pains had disappeared, and the function of all affected joints was partly restored. Two years after the onset all joints but one were painless and had a full range of movement; there was no anæmia, no œdema, no albuminuria, and no hepatosplenomegaly. At the age of 19 the girl was symptom-free and leading an active life. The second case, reported by Lush, Chalmers, and Fletcher [2] from the Royal Free Hospital, London, was of a woman aged 44. Five months from the onset the spleen and the axillary and inguinal lymph-glands became palpable. Lymph-gland biopsy established the diagnosis of amyloid disease, which was confirmed by the absorption, within one hour, of 90% of injected congo-red. The spleen, lymph-glands, and subsequently the liver enlarged progressively, and fever continued; there was, however, no œdema and no renal amyloidosis, and the serum proteins were only moderately disordered. No treatment had any effect until crude liver extract was given, when for the first time the patient became afebrile, gained weight, and improved generally. The liver continued to increase slowly, but the spleen and lymph-glands became smaller; and within three months the congo-red test showed less than 10% of dye retained at one hour.

What is the mechanism of resorption in amyloidosis? One possibility is that the natural enzymes, through involvement in the increased protein katabolism and anabolism of a chronic infective or neoplastic process, are insufficient to assure the complete cycle of protein metabolism; and liver extract supplies an essential supplement. A like deficiency might account for the experimental amyloidosis following absorption of excess protein; and it might also explain the occurrence of the disorder in association with the hyperglobulinæmia of antitoxin production and myelomatosis. Possibly the excess amino-acids are then conjugated with chondroitin sulphuric acid, which accumulates in the mesodermal structures of the subendothelial lining of capillary blood-vessels and in the media of arterioles, just as in disorders of lipoid metabolism cerebroside and other cholesterol-phosphatides accumulate in the mesodermal phagocytic cells of the spleen, bone-marrow, and liver. In the rheumatic group of diseases collagen undergoes focal degenerative change—the so-called "fibrinoid" necrosis—and this might be considered the source of the excess glycoprotein later deposited as amyloid material. In rheumatoid arthritis associated with amyloid change, enlargement of lymph-glands and spleen has been noted; and, in accordance with the view that gamma-globulin is a product of lymphoid hyperplasia, this enlargement is thought to determine the hyperglobulinæmia and amyloidosis. It is to be noted, however, that Lush, Chalmers, and Fletcher detected amyloid disease in only one of their 200 cases of rheumatoid arthritis with altered plasma protein; and this one case showed the smallest deviation of all from normal. Whatever the mechanism, however, liver extract deserves a wider trial in the treatment of amyloidosis.

1. Kuczynski. Cited by Muir, R. Textbook of Pathology. London, 1941; p. 156.
2. Lush, B., Chalmers, I. S., Fletcher, E. *Ann. rheumat. Dis.* 1948, 7, 225.
3. Yeoman, W., Wilson, J. V. *Brit. med. J.* 1947, ii, 483. Hill, L. C. *Proc. R. Soc. Med.* 1948, 41, 607.
4. Trasoff, A., Schneeberg, N., Scarf, M. *Arch. intern. Med.* 1944, 74, 4.
5. Grayzel, H. G., Jacobi, M. *Ann. intern. Med.* 1938, 12, 39.

W.H.O. PLANS FOR THE FUTURE

UNDAUNTED by the withdrawal of the U.S.S.R., Ukraine, and Byelorussia,[1] the executive board of the World Health Organisation spent a large part of its third session of just over two weeks in discussing the programme and budget for 1950. At its second session last October, the board had given Dr. Brock Chisholm, the director-general, a mandate to prepare a Bold Look Budget for 1950, and this had been done to the tune of over 20 million U.S. dollars.[2] Though, as was repeatedly emphasised, the members of the board—as individual technical experts not representing their countries—were concerned with needs and programmes rather than with the size of the budget which member States were likely to approve at the Assembly, the probability that a budget of about 20 million dollars would not be acceptable was bound to colour their discussions. Hence they grasped eagerly at an ingenious plan put forward by Dr. van Zile Hyde (U.S.A.) whereby the regular budget would be increased from between 5 and 6 million dollars to just under 8 million and a supplementary operational budget of 9 million would also be presented to the Assembly, to which countries would contribute according to their resources and generosity and not according to their scales of assessment. Nevertheless, some hard battles were fought, and reductions were made in a number of programmes, notably in mental health and in supplies. The attack on the mental-health programme produced a most interesting debate, ending in a programme somewhat reduced but not by so much as had been suggested. The proposal that W.H.O. should provide medical supplies unobtainable by the countries themselves, and additional to those necessary for the work of the advisory and demonstration teams supplied by W.H.O., was

1. *Lancet*, Feb. 26, p. 355.
2. *Ibid*, 1948, ii, 897.

Digitized by Google

supported by the members from Eastern European countries. The discussion was embittered by their charges against the U.S.A. of discrimination in the granting of export licences: indeed, there were signs that the continued coöperation of the Eastern bloc with W.H.O. may depend on the latter's ability to overcome this difficulty. Here again the result was a compromise providing for a much smaller sum of 300,000 dollars for additional supplies, under strict control of the board.

Regionalisation was reported to be going rapidly forward. The resolutions of the first meeting of the regional committee for the Eastern Mediterranean region, held at Cairo in February, were endorsed, including the appointment from July 1 of Sir Aly Tewfik, Shousha, Pasha, chairman of the executive board, as regional director. A working arrangement under which the Pan-American Sanitary Bureau would shortly begin to take over the functions of W.H.O.'s New York office was noted with satisfaction, and the board decided to recommend to the Assembly that a full-scale regional organisation for Europe should be set up as soon as a majority of the European countries stated their desire for it. Meanwhile the Special Office for Europe has concentrated on efforts to get UNRRA penicillin plants in Poland, Czechoslovakia, and Yugoslavia into production.

Field activities in various areas were reported, including continuation of advisory services in China, Ethiopia, and Greece; the allocations of teams and consultants to a number of countries, chiefly in malaria, venereal diseases, tuberculosis, and maternal and child health; the coördination of public-health and epidemic-prevention measures among the refugees in the Palestine area, and numerous joint projects with UNICEF. All in all it can be said that the new-model W.H.O. is running itself in satisfactorily, in spite of disappointments, and it is to be hoped that its owners, the Assembly, when they meet in Rome on June 13, will authorise extended tours in 1950.

CORONARY THROMBOSIS

THE Hunterian Society last Monday heard Dr. William Evans plead—not for the first time—that what is loosely termed coronary thrombosis should be called cardiac infarction; for the infarct giving rise to the familiar and dramatic syndrome is commonly due, not to thrombosis at all, but to blockage of a coronary artery through aortitis. Dr. Evans expressed the view, which was highly acceptable to his listeners, that smoking has no effect on the cardiovascular system: nor, he added, will sudden exertion precipitate infarction from atheroma. In the treatment of the initial pain morphine is the supreme anodyne, and it should not be spared; gr. 1/4 should be given at once, and if the patient does not become pain-free and fall asleep this dose should be repeated after half an hour and, if need be, again after a further half hour; but if this third injection is needed the infarct is large and the prognosis grave. Dr. Evans does not believe that atropine provides any special benefit; and he stoutly denies that nikethamide has any place whatever in cardiovascular practice, even though coroners are gratified to learn that it has been injected. Quinidine should not be administered as a routine; but digitalis should be given where heart-failure arises, as it does in a fifth of the cases. He opposes the use of anticoagulants, to which most patients, in his view, are either resistant or sensitive. Six weeks is probably about the right period for the patient to be confined to bed. As to long-term therapy, half a tablet of trinitin chewed before exertion that normally induces angina will often prevent its onset; thus anginal attacks may be reduced from, say, 6–8 per day to 2.

Discussing long-term management, Dr. Geoffrey Bourne advised measurement of the heart size as a guide to treatment; if the heart is not much enlarged and if on serial examination it does not increase in size, then the prognosis is correspondingly better and treatment can be more vigorous; with an enlarged heart, even if the patient is symptom-free, treatment is unlikely to prove so satisfactory. The second guide is the blood-pressure, and particularly the diastolic pressure; the chance of success in treatment is best with a fairly normal pressure. The patient should be encouraged slowly to find his own physical level. Dr. Bourne imposes no veto on the consumption of alcohol, or of food provided that the stomach is not overfilled; but he is more wary of tobacco than Dr. Evans, having seen two patients who reported that before the attack the warning retrosternal pain was induced by half a cigarette. Fat patients should set about reducing their weight. A common sequel to infarction is effort syndrome, with a heavy precordial pain lasting 2–3 hours at a time, and possibly aggravated by exercise and associated with pain down the arm; here careful history-taking should be followed by reassurance. The intelligent patient should be told what is happening, and that healing will take time. Incalculable harm can be done by hestitation and pessimism; possibly egotistical pleasure underlies the grave head-shaking which drives patients into chronic invalidism. The attitude has to be one of unwavering optimism: the patient should be told not about his chance of dying but about his prospect of surviving.

Mr. George Mason related his experiences in establishing a collateral extracardial circulation, and illustrated his theme with a film of patients engaged in impressive physical exercises several years after omentopexy. It was left to Dr. Jenner Hoskin, who some twelve years ago took a leading part in a similar discussion by the same society, to recall that except for minor advances little had been added in recent years to the understanding of cardiac infarction.

F.R.S.

AMONG the fellows of the Royal Society elected on March 17, we note with pleasure the name of Wilson Smith, professor of bacteriology in the University of London at University College. Though this year there is only one doctor on the list, several of the new fellows have won distinction by work which is closely associated with medicine. They include: F. W. R. Brambell (University College, Bangor), E. B. Chain (University of Oxford), Kenneth Mather and P. B. Medawar (University of Birmingham), W. T. J. Morgan (Lister Institute, London), D. A. Scott (Connaught Laboratories, Toronto), and F. G. Young (University College, London).

THE KING'S HEALTH

THE latest bulletin (March 21) issued from Buckingham Palace before we went to press was as follows:

The King's recovery from his operation has been uneventful.

Instrumental tests have confirmed the substantial improvement in the blood-flow to the right foot which had already been observed clinically after the operation.

MAURICE CASSIDY
THOMAS DUNHILL
HORACE EVANS
J. R. LEARMONTH
J. PATERSON ROSS
JOHN WEIR.

Dr. WILLIAM JOHNSON, consulting physician to the Royal Liverpool United Hospital, died on March 15 at the age of 63.

We also regret to record the death of Dr. G. M. STOKER, of Mitcham, on March 21 at the age of 50. Last year Dr. Stoker succeeded the late Mr. G. F. Stebbing as chairman of the council of the Medical Protection Society.

Digitized by Google

Special Articles

THE REFLECTING MICROSCOPE *

ROBERT BARER
M.C., M.A. Oxfd, M.B., B.Sc. Lond.
ALAN JOHNSTON, LAWRENCE, AND MOSELEY RESEARCH FELLOW OF THE ROYAL SOCIETY; UNIVERSITY DEMONSTRATOR IN ANATOMY, OXFORD

THE last fifteen years have seen the birth of several advances in microscopy which can only be described as revolutionary. The reflecting microscope must take an important place among these discoveries, not merely as a competitor to the refracting microscope but also because its possible applications are so vast and so novel that, though great territories of research are opened up, it is unlikely that they will be fully explored in our lifetime. Some of the main lines of research already undertaken with this instrument are briefly described here.

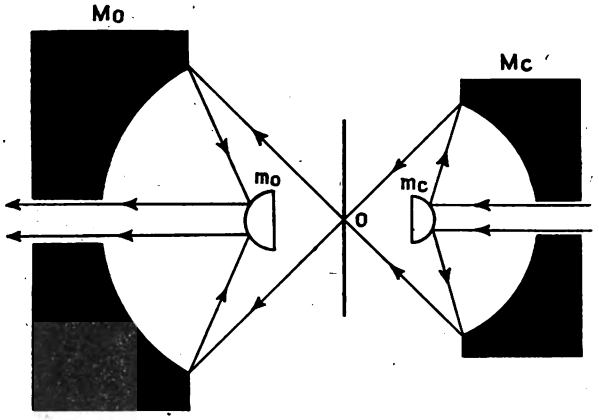


Fig. 1—Diagram (not to scale) of the present Burch microscope. The two large mirrors M_C and M_O are aspherical. Immersion components are available but not shown.

Reflecting microscopes have been constructed in various countries, but far the most promising type is that built by Dr. C. R. Burch, of Bristol (Burch 1947, Barer 1947). This differs from most other types in that aspherical mirrors are used in an attempt to ensure the highest optical performance. It is relatively easy to construct a reflecting microscope using spherical mirrors, but the numerical aperture (N.A.) of such an instrument cannot readily exceed 0·5 without the introduction of serious distortion due to spherical aberration. The use of aspherical surfaces enables the N.A. to be increased up to about 0·95. Unfortunately such mirrors require an unusual degree of technical skill for their construction, and it is rather doubtful whether they will ever be mass-produced.

The optical system of the microscope now in use is shown in fig. 1. The objective consists of a small spherical convex mirror m_o and a large aspherical concave mirror M_o. The N.A. of this system is 0·65. The condenser is similar, with N.A. 0·58. The mirrors are made of speculum metal accurately figured by hand. They are coated with a very thin reflecting layer of aluminium.

APPLICATIONS MAKING USE OF THE LONG WORKING DISTANCE

In the present instrument the clearance between the object and the small mirror m_o is 13 mm. This could be increased to about 20 mm. without much difficulty. A lens microscope of similar N.A. has a working distance of less than 1 mm. This feature greatly facilitates microdissection. For example, organs such as the liver, spleen, kidney, and brain of a living anæsthetised animal may be examined in situ at a working distance which permits operations under high magnification. Microdissection of cells by phase-contrast illumination is also simplified, and indeed the whole range of micromanipulative techniques is greatly extended.

Another application of considerable promise is the use of the instrument as a high-power skin or capillary microscope.

APPLICATIONS MAKING USE OF THE ACHROMATISM OF THE SYSTEM

It is well known that the focusing properties of a lens system depend on the colour or wave-length of the light used. This is not the case in a reflecting system, which is perfectly achromatic. The implications of this simple statement are not often fully understood, but it is this property which has made possible some of the more remarkable applications of the reflecting microscope.

In the first place, once the instrument has been focused with light of any wave-length it remains in focus for all wave-lengths from the far ultraviolet to the far infra-red. The advantages of this for ultraviolet and infra-red microscopy (and indeed for photomicrography in the visible region) are obvious. Straightforward ultraviolet microscopy is valuable on its own account both for the increased resolution due to the use of short wave-lengths and for the selective absorption of certain cellular constituents at some wave-lengths.

This latter feature has been developed by Caspersson (1936, 1940) and others into a method of spectromicroscopy whereby various chemical constituents can be identified and located within cells. This technique has hitherto been exceedingly cumbersome and not altogether satisfactory, owing to the necessity of using microscopes with quartz lenses for the ultraviolet region. As a consequence it becomes necessary to use strictly monochromatic light, to refocus both condenser and objective for every new wave-length, and to use the objective at wave-lengths for which it is not corrected.

The introduction of a truly achromatic system avoids these difficulties and allows the use of a simpler and in some respects more powerful method (Barer, Holiday, and Jope 1949). The principle of this is to project an enlarged image of the object on to the slit of an ultraviolet spectrograph. This enables the entire ultraviolet and visible absorption spectrum of the microscopic object (cell, crystal, &c.) to be recorded in a single photographic exposure. Moreover the use of a suitable source of illumination—e.g., a hydrogen discharge tube—gives the absorption continuously at every wave-length, which it would be impossible to obtain with a refracting microscope.

Many biochemists and pathologists are already familiar with ultraviolet spectrophotometer

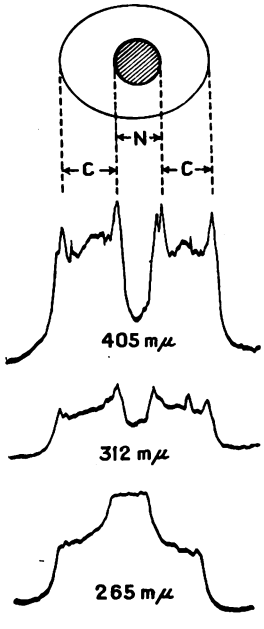


Fig. 2—Absorption of different parts of a frog's nucleated red blood-cell plotted at three different wave-lengths. At 405 mμ (close to the Soret band of hæmoglobin) there is strong absorption in the cytoplasm, whereas the nuclear absorption is weak. At 312 mμ neither nucleus nor cytoplasm shows any special absorption. At 265 mμ the nuclear constituents absorb very strongly, the cytoplasm only weakly.

* This summary of recent work on the reflecting microscope was contributed by request.—ED. L.

Digitized by Google

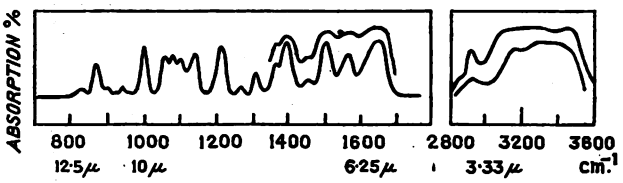


Fig. 3—Infra-red absorption spectrum of a microscopic crystal (weight about 10^{-7} g.) of the anti-pernicious-anæmia factor vitamin B_{12} (from Barer, Cole, and Thompson 1949).

for recording the absorption spectra of small quantities of substances in solution. The reflecting microscope enables similar results to be obtained for solid substances. Apart from the investigation of cellular structure and chemistry (fig. 2), the method promises to be of great value in work on newly isolated substances, such as antibiotics and hormones, which are available in only very small quantities (crystals weighing less than 10^{-10} g. have been investigated).

Recently the spectromicroscopic method has been extended in an entirely new direction. By a modification of the technique employed in the ultraviolet region it has proved possible to investigate the infra-red absorption spectra of cells, fibres, and crystals (Barer, Cole, and Thompson 1949). The infra-red absorption spectrum of a chemical compound is highly characteristic, so much so that it is often referred to by chemists as the "fingerprint of the molecule." Absorption bands in the ultraviolet region, on the other hand, tend to be rather broad and ill defined. There are technical limitations to this method, the most obvious being that it is impossible to work with such small objects as in the ultraviolet region. The resolving power of the microscope decreases as the wave-length rises; hence at 10 μ the linear dimensions of the smallest object which can be dealt with must be about forty times greater than at a wave-length of 0·25 μ (2500 A). Despite this it is possible to obtain infra-red absorption spectra at wave-lengths up to 14 μ on samples weighing less than 10^{-7} g. This has proved useful in the case of newly isolated substances of biological importance. Thus fig. 3 shows the infra-red spectrum of a single microscopic crystal of the anti-pernicious-anæmia factor (Smith 1948). Certain predictions about the chemical nature of this substance have been made as a result of this. Other examples of biological interest, such as the spectra of gramicidin and other antibiotics, and preliminary work on muscle-fibres and nerve-fibres will be found in the paper with Cole and Thompson.

The use of polarised ultraviolet and infra-red light in conjunction with these spectromicroscopic techniques is also promising. These methods may help to elucidate the structure of oriented materials, such as crystals and fibres. Thus the infra-red spectrum may reveal the direction of orientation of such groups as CH, NH, OH, &c., relative to the crystal or fibre axis, and the ultraviolet spectrum may yield similar information about such constituents as benzene rings, purines, pyrimidines, tyrosine, tryptophane, &c. Indeed in favourable cases it may be possible to derive as much or even more information on the structure of organic crystals as by X-ray diffraction methods.

Another type of application in the infra-red region involves the use of a photo-electric image converter system, enabling the infra-red image to be seen on a fluorescent screen. Some interesting results have been obtained, particularly with phase-contrast illumination. Of the numerous possible applications which have yet to be attempted one of the most exciting would be to use it with ultraviolet light of very short wave-length. The quartz microscope cannot be used below about 2000 A because quartz becomes opaque to shorter wave-lengths. With a reflecting system the possibility exists of working down to 1000 A or even less, provided that the mirrors can be made with sufficient accuracy. The use of very short wave-lengths may lead to a considerable gain in resolving power.

As regards the more immediate and mundane uses of the instrument, its performance in visible light is excellent. It has been used for conventional microscopy, as a polarising microscope, and for fluorescence, interference, and phase-contrast microscopy. In nearly every case its performance has compared favourably with the best refracting microscopes of equivalent N.A. Indeed, it is safe to say that the reflecting microscope can perform all that a refracting microscope can, and much more besides.

APERTURE

A question of some importance to biologists is what is the greatest N.A. that can be achieved by a reflecting system. It is well known that the N.A. of an objective without some form of immersion cannot exceed 1. Dr. Burch and his colleagues are now constructing an instrument with N.A. 0·95. It is, however, possible to increase the effective N.A. with a simple immersion-lens component. If such a component is made with a spherical surface whose centre is at the object point, rays pass through it radially so that the achromatism of focus is not disturbed. The N.A. of the present instrument has been increased to 0·98 with such a lens, and that of the instrument under construction will be raised to 1·4 (fig. 4). This is of the same order as that of the best apochromatic lens objectives.

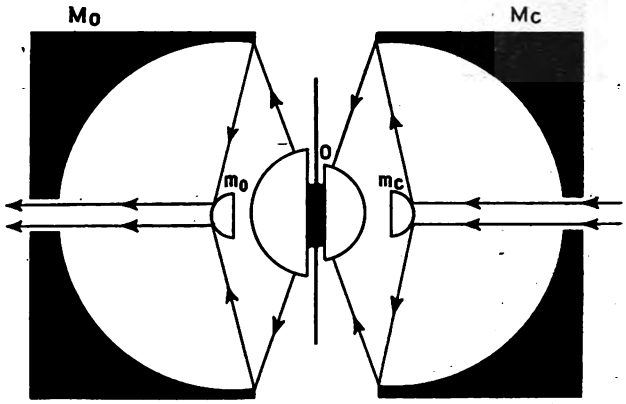


Fig. 4—Diagram (not to scale) of the projected new Burch microscope. All mirrors are aspherical. Note the spherical immersion lenses.

In conclusion, it may be mentioned that the Nuffield Foundation has made a generous grant towards the construction of ten reflecting microscopes of the type already in use. The Foundation has also contributed towards the expenses of the work on the biological applications of the instrument now in progress at the Department of Human Anatomy, Oxford University.

REFERENCES

Barer, R. (1947) *Brit. Sci. News*, **1**, no. 6, p. 12.
— Cole, A. R. H., Thompson, H. W. (1949) *Nature, Lond.* **163**, 198.
— Holiday, E. R., Jope, E. M. (1949) In course of publication.
Burch, C. R. (1947) *Proc. phys. Soc. Lond.* **59**, 41.
Caspersson, T. (1936) *Skand. Arch. Physiol.* **73**, suppl. 8.
— (1940) *J. R. micr. Soc.* 608.
Smith, E. L. (1948) *Nature, Lond.* **161**, 638.

"... On the average a death from tuberculosis robs the community of 24 years of future working life between ages 15 and 65, whereas a cancer death causes a loss of only 5 years between those ages and a fatal accident 18 years."—Dr. PERCY STOCKS, *Tubercle*, March, 1949, p. 50.

Digitized by Google

PROPAGATION OF MOUSE TUMOURS BY MEANS OF DRIED TISSUE

SUCCESSFUL EXPERIMENTS REPORTED

Prof. W. E. Gye, F.R.S., delivering the Imperial Cancer Research Fund lecture at the Royal College of Surgeons on March 22, described experiments on the transmission of malignancy which he has made in collaboration with Dr. A. M. Begg, Dr. James Craigie, F.R.S., and Miss Ida Mann, F.R.C.S.

So many facts have been discovered, he said, about starting cancers by physical and chemical means and about the chemistry and biochemistry of cancer that the position has become confused. The earlier work of the Imperial Cancer Research Fund showed that the familiar tumours of small mammals were pathologically and biologically similar to those of man. E. F. Bashford made it clear that the precipitating causes, such as carcinogens (soot and tar) and physical agents (heat and X rays), were not identical with the originating cause of cancer; even as malnutrition might bring on tuberculosis but the originating cause of tuberculosis was the bacillus of Koch. But Bashford and his colleagues could not find anything, either bacterial or chemical, in tumour tissues that could start a new tumour. Bashford concluded that cancer could be transmitted only in conditions which allowed the continued growth of the tumour of one animal in another animal of the same species, and therefore that the cause of cancer was to be sought in the life processes of the cells, normal or malignant.

In 1911 Peyton Rous proved that a cell-free extract of a sarcoma in a chicken contained an agent which could produce a similar sarcoma in another chicken. Since then electron microscopy has shown that this agent is a virus which exists in the tumour cells. Further, it is now known that, when malignancy is transmitted by such a virus, the type of cell of the new tumour is the same as that of the original tumour, even as with a grafted tumour. This fact illustrated the specificity of the virus. On the other hand, an immune serum made by injecting virus from one kind of tumour will neutralise the viruses of other kinds of tumour, showing that there is an antigenic element common to all of them. Though further experiments showed that the tumours of chickens, the adenocarcinoma of the frog, the Shope papilloma of the rabbit, and the mammary cancers of inbred mice were due to a virus, all attempts to produce tumours in small mammals and man by injecting filtered extracts were unsuccessful, and it seemed that there must be two entirely different kinds of malignant tumours. It was therefore necessary to test this apparent inability to transmit malignancy by a virus.

Dr. Gye and his colleagues decided to reinvestigate this question. Two previous observations seemed to be important. In the first place both Bashford and Ehrlich had shown that the spindle cells of a spindle-cell sarcoma which arises in the stroma of a malignant mammary cancer arose from normal stroma subjected to the influence of the epithelium. This fact suggested that something (possibly a virus) passed to the normal cells and produced malignancy in them. Secondly, Ehrlich discovered in 1907 that sarcomas and carcinomas could be kept at a temperature of −10°C for two years and still give rise to fresh tumours on transplantation. Most workers concluded that the cancer cells had survived this long freezing, but W. Cramer believed that they had been destroyed. A few years ago Miss Ida Mann, using homozygous mice, proved that normal embryonic tissue was destroyed by less than an hour's exposure to a temperature of −79°C; yet malignant tissues kept at that temperature for more than a year can still produce malignancy on injection into another animal.

Next, Dr. Gye and his colleagues examined histologically grafts of malignant tissue, at different intervals after grafting, to see whether the new tumour arose from the graft or from the recipient's own tissues. They found that frozen grafts contained no normal cells, all being necrotic. New sarcomas were formed from the host's capsule surrounding the graft.

Meanwhile Dr. Craigie and Dr. Begg studied the results of other assaults on the cancer tissue apart from freezing. For instance, the tissues were minced finely enough to pass through a needle of the finest bore (26 gauge) and were subjected to the lethal action of various diluents, such as distilled water, 40% glycerin, and 40% glucose. These operations did not prevent such tissues from producing a tumour when injected into another animal. On the other hand, peptone, which would not be expected to be lethal to the cancer tissue, inhibited the growth of a new tumour.

Finally, with a new apparatus devised for the purpose, the cancer tissue was completely dried before injection. Hitherto no mammalian tumour had been propagated by means of completely dried tissue, but after drying by the new method three mouse sarcomas have been successfully transmitted: (1) a sarcoma which had been produced by injecting methylcholanthrene; (2) a sarcoma of the inbred strain R3 which had arisen by infection of the connective-tissue stroma of a carcinoma; and (3) a sarcoma of the homozygous strain C3H which had arisen during the transplantation of a sporadic mammary carcinoma. Strangely enough, better results were obtained by freezing the dried tissue. Possibly (Dr. Gye suggested) the low temperature denatures an inhibitory protein, thus freeing the virus.

The implication of these experiments, he concluded, is that the sarcoma of chickens and other easily filtrable tumours can no longer be regarded as a class separate from most other tumours; and, since the chicken sarcoma has been proved to be due to a virus, the mammalian tumours must be considered to be due to viruses. The question remains to be decided whether the viruses are of intrinsic or extrinsic origin—i.e., are the viruses made by the infected cells or not? This question is part of the general problem of the nature of viruses.

ON KNOWING MEN

PROFESSOR SPENCE'S ADDRESS

Dr. J. C. Spence, professor of child health in the University of Durham, speaking on March 18 at the conference on mental health arranged by the National Association for Mental Health, said that fully to understand the nature of our fellow men may be beyond the reach of most of us, life being short and the art too long for that. Nevertheless, doctors and nurses, because of the intimate character of their professional work, need particularly to understand the individual and to consider his feelings.

FOUNDATIONS OF UNDERSTANDING

The basic understanding which comes by the process of trial and error in the experience of close human relationships; and finds expression in proverbs and precepts, is the currency of our daily lives and is measured in terms of harmonious living with family and friends. Expert understanding of abnormal types comes by particular study and trained observation. Specialised understanding of one or other aspect of the individual is seen, for example, in the industrialist who selects with unfailing skill a man for a particular job, by understanding that quality for which he employs him, though outside these limits he may go quickly astray. The capacity to understand a person in all of these three ways depends on our sensitivity, our intelligence, our experience, and our training; but not on these only. To understand we must see clearly, and we do not see clearly if

Digitized by Google

we are blinded by envy, pride, jealousy, fear, or greed. The doctor and the nurse, then, must gather their experience and train their powers of observation in a spirit of sympathy, charity, and magnanimity; and the capacity to understand people is therefore on another and perhaps higher plane than mere scientific observation. Understanding begins in childhood, that apprenticeship to life, and this early experience is the richer if it is gathered in the companionship of other children of different types and different ages, in the streets, in the hedgerows, or on the village green, free from the restriction of adult supervision. We begin to learn by withstanding the little tyrants, by sharing loyalties, by enduring exploits, by proffering help, by accepting aid. If some of us failed to get this experience in childhood, it may be because we lived too much in a life arranged for us by adults. "I am not here pleading for the go-as-you-please type of education, but the child must have its freedoms, and its solitudes, if its experience is to be transmuted into an understanding of individuals." Nevertheless, this transmutation will be the better if the experience is gathered against the background of a wise parental discipline and a family code of morals. This apprenticeship to understanding goes on through adolescence, but even on the verge of manhood it is still incomplete.

THE PURPOSE OF MEDICINE

Does a doctor need to understand the individual more than the lawyer, the teacher, the industrialist, or the administrator? If life were merely a matter of economics and jurisprudence we would not say so. But fortunately the good life is not a matter of economics: it is a matter of manners, of ethics, and of moral philosophy, with charity as its safest guide for most of us. Looked at in this light the doctor, if he is to work with success, needs to know the individual with basic, expert, and specialised understanding. He sees men of all ages from childhood to senility, in the confidence of full health and in fear of sickness, near the noon of day when courage is at its height, and in the small hours of morning when it so often ebbs away. Not only must he understand the individual but he must understand him in many of these variations from the norm.

The real work of a doctor is not an affair of health centres, or public clinics, or operating-theatres, or laboratories, or hospital beds. Techniques have their place in medicine, but they are not medicine. The essential unit of medical practice is the occasion when, in the intimacy of the consulting-room or sick-room, a person who is ill, or believes himself to be ill, seeks the advice of a doctor whom he trusts. This is a consultation, and all else in the practice of medicine derives from it. The purpose of a consultation is that the doctor having gathered his evidence shall give explanation and advice. The explanation may be that the patient has appendicitis, and the advice may be that he should go to such and such a hospital to be operated on, by such and such a surgeon. But the purpose of the consultation is not the diagnosis or the technical treatment; it is the explanation and advice. The explanation is pursued further with what the Greeks called *pronoia*, which is something more than prognosis. The doctor uses his understanding of the individual and of his disease to prepare him and his near relatives for the hospital, for the technical treatment in the hospital, and for his life after hospital. Intimacy, courtesy, and understanding are required in this work. In a proper consultation no third person should be present other than the parents or near relatives of the patient.

TEACHING THE ART OF CONSULTATION

If this is, in fact, the purpose of medicine how are we to train our students? Can we in fact teach the art of consultation?

Those who do not like this way of medicine, who are more interested in things than in people, will find their place by working in laboratories or as technical therapists. For the others, many pick up the art of sympathetic and wise consultation without any formal training in it. Perhaps they have come under the influence even for a brief time of a wise practitioner of medicine who gives them a pattern; perhaps it is the fruit of inborn sensitivity and of good manners learned in childhood. But in the training of our doctors and nurses we must act in the belief that to understand the individual is an art which can be cultivated, so it is worth our while to demonstrate it.

For medical students, the art of consultation is best demonstrated in the outpatient departments, though it is not always easy to arrange a form of outpatient consultation in which students can share. In most cases it is impossible to conduct a satisfactory consultation in the presence of a third person, but in Durham University, Professor Spence said, they do what they can. Consultations are given by the most experienced members of the staff and two or three students are allowed to listen with as much self-effacement as possible. They observe the greeting, they hear the questioning, they watch the examination, and finally they listen to the explanation and advice. They do not examine the patients. Once they have accepted this rôle they appear to appreciate the occasion: they share in the sense of relief when the explanation removes brooding fears; they may even feel a little of the anguish when a tragedy unfolds itself. After the patient has left the room discussion centres *on the consultation*, while the pathology and diagnosis of the disease is commented on only briefly if at all. The choice of words used in explanation is reviewed; the restraint is recalled. An experienced teacher can thus reveal to a student a great deal about individuals, and about life itself, which cannot otherwise be seen in hospitals. Students are warned of the difficulty of demonstrating the art of consultation in the presence of a third person. They are told that they must make three diagnoses: of the disease, of the concept or fears of the disease in the mind of patient or parents, and of the patient's capacity to understand the explanation and follow the advice. It is the patient's privilege to be interviewed without students being present if he so desires; Professor Spence finds that less than 10% demand this privilege, and for these it is readily provided.

Students are quick to see the significance of consultation; but lest their hopes fly too high, he reminds them that between these vivid episodes there will be a great deal of dull certificate writing. He illustrated the value of consultation and *pronoia* with examples.

A woman seeks advice about her mentally defective baby. She herself says nothing about its feebleness of mind; she may know it or suspect it, but she talks of other things. The doctor estimates her notion of the situation, her attitude towards it, and her capacity for dealing with it. This enables him to choose the right questions with the right words, and to frame his explanation and advice. But beneath this encounter there is much the doctor is aware of. The woman probably carries a deep sense of guilt that the child's condition may be due to something she has done or left undone during her pregnancy—for example, she may have used abortifacients, but she fears to confess it. The doctor knows this without being told, and takes care to remove this corroding guilt by saying, in the course of his explanation, that the child's feebleness is due to no fault of hers, or to anything she may have done during pregnancy. He may not be able to cure the child, but he can cure the mother's morbid sense of guilt. Again, a misheard phrase may frighten a patient. He recalled using the phrase: "One in a thousand, please, nurse" when referring to a 1 in 1000 dilution of a test fluid. The mother heard this as "A one in a thousand disease, nurse." He only learned by chance of the anxiety this caused her.

Digitized by Google

TEACHING THE NURSE

Our system of training attempts to introduce nurses to the need for understanding the individual patient; but, understanding being an art, is it better learned by example and exercise than by precept and lectures. The most valued lessons will come from observing their ward sisters and the doctors. The ultimate responsibility for the care and nursing of the sick is, or should be, in the hands of the ward sisters: in this the doctors are responsible to her and not she to the doctors. She may undertake a few practical exercises to demonstrate the need for understanding to her nurses.

She may, for instance, change from time to time the position of the patients in the ward to give them better companionship, not only to simplify technical treatment. To do this often in the presence of young nurses is a good way to demonstrate the need for understanding. A second exercise is to teach them to enter and leave a room quietly. This is better demonstrated in an out-patient consultation service than in wards. The third exercise is in the smile of greeting, nature's most elementary instrument to open the way to understanding. A nurse's sour look may be as harmful as a septic finger, and if she cannot overcome it, she had better not be a nurse. The fourth is the choice of conversation. To be interested rather than interesting is the first rule of conversation. A man's primary interest is in himself, next in his family, next in his immediate surroundings, next in his work, next in his hobbies. A woman's interests are of a slightly different order. Conversation directed to these interests may be flavoured with a little cajoling, teasing, sympathising, or serious attention as befits the occasion. Just as it is a chastening experience for any broadcaster to have his recorded voice played back at him, so it would be a corrective for a nurse to have her small talk recorded for her hearing. It might then subdue the bright young thing who is constantly cheerful in brittle talk however sombre the occasion; the girl with the perpetual cliche about the nice flowers, and the baby talker with her "How's your little tumsie wumsie today Dad?" Other exercises are in the use of telephones and the interview of relatives. Tiresome inquirers are probably fewer than 5% and we must adjust ourselves to the other 95% of earnest harassed people who come to hospital for news.

Dr. Spence added that some of the wisest, most courteous, and most humane of beings he has ever known have been nurses with whom he has worked: they indeed have had a basic understanding, an expert understanding, and a specialised understanding of the individual.

NEW ZEALAND HOSPITAL SALARIES

FROM OUR NEW ZEALAND CORRESPONDENT

THE salaries of doctors engaged in full-time hospital practice in New Zealand are improved under regulations gazetted on March 3.

On the administrative side, superintendents-in-chief (where more than one institution is concerned) are to receive £1900–2250, and superintendents from £1650–1900 to £1250–1500 according to the size and function of the hospital concerned. In some cases an extra sum of up to £100 per annum is allowed where specialist duties are included.

Full-time specialists are graded and paid as follows:

	£
Principal specialist in employ of Auckland, Wellington, North Canterbury, or Otago boards	1750–2000
Senior specialist	1400–1700
Junior specialist	1050–1350
Medical officer of "special scale," six grades—	
from	1400–1550
to	800– 950

The ranks depend on higher qualifications and/or length of service in the specialty, and the individual must be designated to the particular rank by the board concerned, with the approval of the Minister.

In almost all cases these scales represent an improvement on present rates, and will go a considerable distance towards ameliorating the harsh disadvantages hitherto besetting the full-time officer, as against the general practitioner under Social Security and the specialist in private practice. It should now be possible for hospitals to obtain and retain well-qualified men on their full-time staffs. Two criticisms may be made:

1. The administrative officer is still regarded as more valuable than the full-time specialist clinician at the corresponding level. At present few administrative officers can compare with the clinicians in higher qualifications, and almost none have undergone special training for their work.

2. Although regulations governing annual holiday leave (four weeks) and sick leave are attached, nothing is said about periodic study leave, either for short visits within Australasia, or the longer leave of 4–6 months, preferably with air travel, desirable at 4–7 year intervals. This is a sine quo non for high-grade specialist service in New Zealand, and it is to be hoped that substantial help will be planned for this purpose in the near future.

Disabilities

26. ENURESIS

As far back as I can remember, I used to wet the bed. It happened intermittently and inexplicably. My parents tried to cure me by various means. At first they punished me. This sometimes made me miserable, but didn't deeply worry me, for I knew it wasn't my fault and that they would find this out in time, as they did. Then they consulted doctors and tried waking me at night, and limiting the amount I drank in the evening, and a number of more obscure treatments which I have since forgotten. None of them had any effect one way or the other.

I was an only child, an active-minded little girl, with a sensitive, rather unstable mother and a perfectly dependable father. I was sometimes bewildered and upset by my mother's emotional reactions, and often afraid when my restless mind urged me into unknown country; but difficulties spurred me on to understand myself and other people, and I came to no serious harm.

When I was eight years old I was sent to a co-educational boarding-school, and there it was thought that firm treatment would soon cure me. I slept in a dormitory with nine other small girls, who found my trouble a pleasant excuse for persecution. The staff made me wash my own sheets and blankets by way of character training; if they had supplied me with an efficient rubber sheet, everyone would have been saved a lot of trouble. The thing that upset me most was that the scandal soon spread round the school, and the boys used to call out "little wet-her-bed" as I went by. It took me some time to come to terms with the opposite sex after a start like that.

A few years later I happened to get infantile paralysis, which affected my hands and arms and also left me with a weak back. This was, and sometimes still is, rather a nuisance, but has never prevented me from doing anything that I really wanted to. Compared with the disabilities which the bedwetting imposed, it was negligible.

As a result of the illness, I was away from school for four years. When I went back there were no children left who remembered my past history, and the staff assumed that I was cured. I was again put to sleep

Digitized by Google

in an open dormitory, but this time I was determined that no-one should find out about the bedwetting, and no-one ever did. Often I escaped discovery by a hairs-breadth, and some of the devices I adopted scarcely bear thinking on now, but they served their purpose. It became a game of skill; concealment was merely an expedient, and I had no deep sense of shame about it. I made plenty of friends, and thoroughly enjoyed those last two years at school.

By the time I went to college I had invented better ways of dealing with the practical problem, though it was a confounded nuisance, especially when living in lodgings or staying in other people's homes. It limited my social activity in many ways, but I learnt to put up with it.

I had nearly finished my professional training when a doctor who was seeing me for something else found out about the bedwetting and told me that it was certainly a neurotic symptom. This shook me to the roots. I had been through my fair share of adolescent emotional upheavals and had been forced at the same time to shoulder heavy family responsibilities and to deal with difficult and distressing situations. In spite of this, I was absolutely determined to make myself into a well-adjusted person, and I thought I hadn't done too badly. I believed that all I needed to put my emotions into perfectly good running order was a convalescent period of normal social life. I believe now that I was right. Unfortunately I couldn't prove it, and for the first time I became deeply ashamed of my complaint.

After an attempt at psychotherapy which caused a violent disturbance and nearly threw me right off my balance, I was left to put the pieces together again. This I managed, luckily, just before the most testing period in my life began. At the same time, for reasons which I now know to have been irrelevant, the bedwetting cleared up. I concluded that the neurosis theory had been right, but that I was now cured. Then the trouble began again. In succeeding years it was as bad as it had ever been before, and worse, and sometimes it brought me very near to despair. I was branded in my own eyes as a chronic neurotic, and this implied to me a disfigurement far worse than any physical deformity. I continued meanwhile to make steady progress in my profession and to lead as normal a social life as one could expect in war-time London; but the shadow remained. However well I might conceal it from others, it was still my belief that, by my own standards, I had completely failed to make a satisfactory job of myself.

* * *

I can never permanently accept something which doesn't make sense. I wanted to understand why I was sometimes better and sometimes worse, but the theory did not help me to make a pattern of the facts. I finally looked back over my life story to see whether there was any common factor which linked up my occasional remissions. One point stood out at once. Whenever I had to stay in bed, whenever I had a long period of leisure with as much rest and sleep as I felt inclined for, I was free from the trouble. There had never been any exception to this rule. It did not explain the odd fluctuations at other times, but it gave me a clue. At the same time I picked out the times when emotional strains and conflicts had been most severe, but these were not consistently linked with bedwetting. The lack of connexion was much more striking. I remembered the long period of idleness, unhappiness, and gloom, which ended in shattering personal tragedy and acute crisis. I had been at the time in a foreign country with no help at hand, and my life was threatened in a peculiarly unpleasant way. I just had to cope. I was free from bed-wetting during the whole of that time. In happier days, when I was leading a more active life, the trouble returned.

When the relevance of this dawned on me, I said: psychiatric fiddlesticks! and went to see another doctor. I was advised to take ephedrine, and it worked like a charm. In my first enthusiasm I thought that I had come to the end of my difficulties, but there were pitfalls ahead.

My working life, just then, was fairly strenuous. I was fully occupied in keeping pace with my normal work, and at the same time I undertook, perhaps unwisely, to write a book to other people's specifications. I found that, by adjusting the dose of ephedrine to suit the load, I got on quite well. I took it before I went to sleep, and the trick was to flatten out the first deep trough of sleep during which the bedwetting would happen if it happened at all. As the load went up and as I grew more tired, the dose had to be increased to be effective. On the other hand, if I misjudged and took too much, I didn't get any sleep. Quite suddenly I reached an exhausted stage where sleep deserted me for nights on end and I developed, among other things, a feeling of acute irrational panic. I cut out the drug completely for a week or so, and was more careful afterwards, realising that the cure might be worse than the disease. I learnt to compromise between the dose that would certainly prevent bedwetting and the dose that would probably let me sleep. There were no more acute disturbances until a couple of years later when I topped off a week of heavy dosing with a night journey in a sleeper. The results were unpleasant while they lasted, and I decided that the game had gone on for long enough.

By then I had been cutting down my sleep artificially for about four years. I had lost weight, was always tired, and took a disproportionate time in throwing off minor infections. My normal sleeping rhythm had disappeared, and, the more tired I was, the more sleepless I became. Otherwise my health was good; but my output of spontaneous creative work had fallen to nil, and my morale was low. I suspected that I was neurotic after all.

When I had given up taking ephedrine for some time, my normal sleeping rhythm began to come back again, and it occurred to me to wonder whether the drug could serve me in a different way. Since I knew how to control the bedwetting artificially, I might be able to find out how to do it by natural means. It was such a faint glimmer of feeling, it scarcely deserved the name of hope, but it was something. I said to myself at intervals "If you can't manage yourself, no-one else can," and I got there in the end.

* * *

It took me some time to fit the facts into a logical pattern; but once I had done so, success came more quickly and more completely than I had ever dared to hope. It would take too long to describe all the steps in detail, but I will give my conclusions briefly. I assume that my trouble is either a disorder of sleep or a defect—a faulty connexion, one might picture it—which shows up during sleep. The remedy is *never to sleep too deeply*. To achieve this I had to understand and then to control my sleep.

The first thing which makes me sleep too deeply is physical exhaustion. This is the most important cause, and if I lived a life of leisure there would be no problem—but I have work to do. In practice I try to limit the kinds of physical exertion which exhaust me, remembering always that my back is the weak spot which gives the greatest trouble. I may safely walk long distances over rough country, because this uses my best muscles; but I am cautious about house-decorating or digging in the garden. If I find that I have overstrained myself, I can prevent the bedwetting sequel by taking ephedrine. This is invaluable in emergency, but I take good care that it isn't needed often.

The mental factors which affect my sleeping rhythm sometimes run parallel to the physical ones, but they may

Digitized by Google

equally well act in an opposite direction. Once I realised this, an apparently nonsensical series of events sorted themselves into an orderly sequence of cause and effect. Other things being equal, lack of sufficient intellectual stimulus makes me oversleep. This is unlikely to affect me again, but ephedrine can be a good corrective; it certainly helped to get me out of depression and apathy and into a fit state to take myself in hand. Mental activity of a creative kind at first reduces sleep, but may lead to oversleeping in the end. It needs care and understanding to control this, but it is not really difficult. If I get absorbed by some exciting problem, or if I am writing something which takes hold of my imagination, I cannot rest completely until I get to the end of it. I sleep less, eat less, and cannot easily give more than half my mind to anything else. When it is finished I sleep soundly and eat like a horse. If I can keep the machine in good running order, the alternation of phases is a smooth and pleasant one. I get into trouble at once if I overdrive myself during an active phase.

Excessive mental activity on top of the physical demands of daily life acts like an overdose of ephedrine. Unlike the drug, however, it can't be continued indefinitely. Under normal conditions, if I run myself for too long at too high a voltage, I blow a fuse. After getting scarcely any sleep for a few nights I suddenly black out and sleep very heavily indeed. This always causes bedwetting, but on the other hand it is a valuable safety device. I start again as good as new. If I went on using a drug to prevent it, I should crack up completely in the end. Now that I have grasped the principle I can prevent myself from getting near the blackout stage, and a day off walking on the hills is better therapy than any sedative. Occasionally I prefer to put up with bedwetting in order to deal with an emergency load, but this is a matter of choice. Accidents don't happen, unless I have been careless.

* * *

It is part of my job to encourage and help people in solving their personal problems, and to train others to do this. A lurking doubt of my own mental fitness has therefore been a particularly serious and irksome handicap. I had gained practical control of my condition for some time before I dared to believe in my success and to accept its implications. When I reached that point I became, instantly, effervescent with relief. I never realised how heavily the burden weighed until it was removed.

As far as I can see, on the basis simply of personal observation, mental activity depends on a combination of physical, intellectual, and emotional stimuli, and too much or too little of any of them may interfere with mental comfort and disturb normal sleep. I realise that lack or sudden loss of emotional support or an acute emotional disturbance could well be an important factor in some bedwetting, but it seems to have had little relevance to mine. I had been led to suppose that my desires and my affections were my weakness, and that disasters had finally wrecked me. I am sure that this is not true. Certainly I have known loneliness and deprivation, fear and sorrow, but these are normal strains for any normal mind. I have also known frustrations and resentment and felt the full stress of sex and love. I was at times troubled by strong feelings in the days when I had to ride them on the curb, but I have now learnt to be on friendly terms with my emotions and they serve me well. I believe that in this respect I am quite tough and fully normal.

I can only say: judge me by my results. I now sleep easily and wake naturally, my resistance to infection is good, and I'm scarcely aware of my defective muscles. I cannot fairly assess the quality of my work, but others will have noticed an improvement. The human and the scientific problems challenge and delight me, and my output has much increased for about half the effort previously put in. I have a sense of comforting and irrepressible physical well-being, and I am radiantly happy. My tendency to bedwetting remains exactly the same as it has always been; but in learning to overcome it I have, accidentally, transformed my life.

I am thirty-four years old and I am still unmarried, but the present reasons for my single state are scarcely relevant. In the past I felt that marriage was out of the question, and it seemed at the time a crushing disability. I never believed in the theory that marriage would cure me. Apart from obvious practical considerations, I did not consider myself fit to be a wife and mother unless I could prove my stability to my own personal satisfaction. I am reassured on that score now. If my path should chance to lead towards marriage, well and good. If not, it is no matter. Happiness, after all, has scarcely anything to do with getting what we want; it grows from making something out of what we've got—and joy cometh in the morning.

Parliament

Analgesia in Childbirth

IN the House of Commons on March 15, Mr. ANEURIN BEVAN, Minister of Health, stated that at the end of 1947 more than 7000 of the 16,000 midwives then practising were trained in the administration of analgesia. During 1948 practising midwives were trained at the rate of 240 per month and at this pace training would be completed in two years. In 1938 analgesia was administered by domiciliary midwives in England and Wales in less than 1200 cases; in 1944 it was administered in 5100 cases, while in 1947 domiciliary midwives were able to give this relief in almost 44,000 cases. Returns for 1948 were not yet complete, but in 72 areas analgesia was administered in 16,500 cases in the six months of 1948 during which the National Health Service was in operation, compared with 9100 cases in the last six months of 1947.

It was the Government's policy and determination, he continued, to secure that full facilities were provided as quickly as possible for women to have analgesia in childbirth. In so far as it was necessary to ensure that sufficient analgesic apparatus and drugs were provided for the use of domiciliary midwives employed in the National Health Service, that the apparatus was maintained in a proper state of efficiency, and that facilities for transport were provided, he was satisfied that he had all necessary powers to place a duty on local health authorities in these matters. Where the Ministry of Health had thought the provisions for analgesia inadequate in the proposals submitted by the local health authorities the proposals were altered before being approved.

The National Health Service Acts had placed upon the Minister and the Secretary of State the duty of providing an adequate hospital service, and there could be no question but that by reason of this duty an obligation rested upon them to see that proper arrangements were made for the administration of analgesia in their hospitals.

Mr. Bevan was sure that the views spoken with such sincerity and deep feeling in the recent debate would be carefully observed by the authorities concerned with the care of women in childbirth and would create in them also a determination to see that there was no delay or hindrance in making that full provision which both the House of Commons and the Government desired.

Mr. PETER THORNEYCROFT thanked the Minister for his courtesy in making the statement, and welcomed the good news given in his figures, but asked how he reconciled his view that the Analgesia in Childbirth Bill was unnecessary with the criticisms of the Bill made ten days ago, when the House of Commons was told

Digitized by Google

that the measure would be a bad one because it would give such priority to mothers and the analgesia service that it would wreck the National Health Service. Today Mr. Bevan's case was that he was going to provide this by regulation. The National Health Service Act did not prescribe a duty to provide an analgesia service, and how could anyone by regulation turn a permissive power into a public duty?

Mr. BEVAN replied that there was no statutory limitation on the kind and extent of the health service, and therefore there was no need for statutory easement. Limitations were imposed by nature, by medical knowledge, and by the amount of rationed resources the country was prepared to give to health as distinct from other claims.

In further replies Mr. Bevan said that unnecessary anxiety and pain had been caused by misunderstandings which it was his duty to clear up, but he suggested that there were some hon. Members more anxious for publicity than to relieve pain. (Loud Opposition protests.) It was entirely inaccurate to say that under the Health Act the Minister only had permissive power to provide analgesia. The Minister of Health and the Secretary of State for Scotland had the power to modify, change, or enlarge any of the duties imposed on the local health authorities. That included the power to impose on them the duty of using analgesic apparatus. But he was not prepared to select from a general health service one matter for priority. Why should he not give priority to research into cancer or rheumatism? This, he persisted, was not aimed at trying to give the best possible health service, but at exploiting human pain as a political stunt. (Opposition cries of "Shame.")

Replying to further questions, Mr. Bevan reiterated that he was satisfied that he had the powers to impose a duty on all local health authorities in this matter, and, as the figures showed, the duty had been imposed. The figures were improving and they would have enough trained midwives, not in four years as stated in the Bill, but in two years. Every maternity hospital would as soon as possible be equipped with analgesic apparatus. He could not say whether analgesia would be possible for every birth in two years' time, but the Government would do their best to provide it. When a new thing was introduced into the medical world there would always be a number of people who would not benefit immediately. He was anxious that people's expectation of relief should not be unnaturally excited beyond the capacity to relieve them at any given time.

There were more protests from the Opposition in regard to the Minister's accusations, and the Speaker intervened to say that he regretted these provocative statements.

Artificial Insemination and the Law

In the House of Lords, on March 16, in opening a debate on problems of legitimacy and artificial insemination, the Marquess of READING pointed out that a decree of nullity had the effect of bastardising children who might have been born of the marriage. He felt this was a hardship which should if possible be removed. One of the examples he cited was the recent case in which the child had been born as a result of artificial insemination.[1] This practice was growing and the problem could no longer be ignored. It was a matter of public policy that some decision should be given soon, and he asked the Government to appoint a royal commission or a departmental committee to go into this "difficult, dangerous, and debatable matter."

Lord BRABAZON OF TARA, calling attention to the social problems arising from the practice, said that to the ordinary man it seemed extraordinary that the law could give a decision regarding a child begotten by a married man and his lawful wife—even though it be by artificial insemination—to the effect that the marriage had not been consummated and that the child was illegitimate. Insemination by means of a donor raised different problems and he did not believe that in a country of advanced social type such as ours many people would consent to be donors.

The ARCHBISHOP OF CANTERBURY considered that the practice, even though at present on a small scale, was established in this country. According to the findings of the commission[2] which he had set up, A.I.H. was justifiable as it enabled the fulfilment between husband and wife of one of the chief ends of their marriage, but A.I.D. was wrong in principle and contrary to Christian standards. The fact that the child was illegitimate was deliberately concealed and the whole process rested on a basis of deceit and perjury. Either the law must be altered to allow relief from perjury, or A.I.D., he submitted, should be made a criminal offence. The perjury of the husband and wife could not be detected, but what of the doctor who assisted? His Grace was not sure but that the doctor became an accessory to the crime. It astonished and perturbed him that the Medical Defence Union should have advised doctors how to protect themselves professionally against adverse legal consequences. If A.I.D. were made a criminal offence then no doctor could employ it without losing his professional status. It was intolerable morally and socially to allow a practice which depended upon deceit and perjury to continue without either ending it or making it legitimate.

Lord CHORLEY, in his reply, said that the Government believed that to make artificial insemination a criminal offence would have the effect of driving it underground. The practice at present was being pursued on the basis of well-accepted medical supervision. He also doubted whether making it a criminal offence would fit in with the feelings of public opinion. A number of people injured by war service had been able by this means to have families. He considered that the problem was to a considerable extent dominated by the question of fertility, for unless the practice increased substantially it did not amount to a serious problem. He therefore suggested that until the report of the Royal Commission on Population was published—he understood that it was expected within the next few months—important material was lacking without which it was impossible to come to any satisfactory conclusion.

Medical Treatment Abroad

On the adjournment in the House of Commons on March 14, Colonel M. STODDART-SCOTT raised the question of the allocation of currency for this purpose. All were agreed, he affirmed, that some medical conditions which were best treated abroad, in high altitudes and sunshine, and at spas, came into the question. There were also medical pioneers who worked abroad and who undertook cases which lesser men would give up as incurable. The Public Health Act, 1936, which made it possible for local authorities to pay for the whole or part of treatment abroad had been repealed by the National Health Act, and an individual could no longer go abroad for treatment at the public expense. This was now only possible for those who could afford it and who could obtain foreign currency with permission from the Exchequer. In 1948, 914 cases were refused foreign currency, although the treatment had been recommended by a doctor.

The Chancellor of the Exchequer always stated that he had acted upon the advice of the Exchange Control Medical Advisory Committee. It had been stated that there were ten medical members of that committee and that they received for their services £500 each year. They had control of life and death in some cases, but the composition of the committee had never been stated. Was the reason that the committee was composed of medical nonentities or Treasury "Yes-men," or was it composed of distinguished consultants? Most probably, Colonel Stoddart-Scott believes, it was composed of distinguished consultants. If the country could know their names there would be less anxiety among the relatives of people whose applications were turned down. It would also settle some of the unrest among doctors who disliked their recommendations to be turned down by men who had never even seen their patients. He

1. See *Lancet*, 1948, ii, 942.

2. *Ibid*, p. 298.

Digitized by Google

suggested the size of this committee should be increased from 10 to 18 so that one member could represent each regional hospital board area. Before any application was refused the patient should be seen by a member. A larger proportion of Swiss currency should be allocated for the treatment of disease.

Mr. DOUGLAS JAY, economic secretary to the Treasury, said that it had already been agreed with the Swiss government that the amount of currency for this purpose should be increased. There was, he pointed out, no obstacle to people going to any part of the sterling area for health reasons; the only issue was how far the scarcer currencies should be granted for this purpose. There was no question of refusing currency to anybody who would improve his chances of recovery as a result of going abroad. The Exchange Control Medical Advisory Committee did not question the medical facts as stated by the patient's doctor. Their function was to apply common standards in deciding what medical facts justified journeys. On their experience, before this arrangement had been introduced, there was, unfortunately, little evidence that fair standards would otherwise be applied. Nor would foreign exchange be denied to patients already in Switzerland if it could be shown that they would benefit by remaining. The Medical Advisory Committee consisted of 10 leading specialists in tuberculosis and other diseases. It was the wish of the profession, and the members of the committee, that they should remain anonymous. They were not a group of bureaucrats but considered the cases sympathetically and liberally. During 1948 there had been 2907 applications of which 1993 were granted. Of the tuberculosis cases 1009 were granted and only 101 refused. He did not think that the suggested enlargement of the committee would help, because the function of the committee was to make judgment on classes of cases. If they were to have many committees all over the country it would mean that they would have to have experts on each class in order to deal with different types of disease.

R.A.F. Medical Service

Speaking on the Air Estimates on March 15, Dr. S. SEGAL asked the Minister to expand the statement in the memorandum on the Estimates that the campaign against venereal disease had been successful in bringing the rate for 1948 below the rate for 1947. Dr. Segal had always felt that, particularly in peace-time, the medical branch of the R.A.F. offered far more attractions to the young doctor than the medical branches of the other two Services. In the R.A.F. he not only had opportunities of flying but he had more opportunity for research. A great deal of work remained to be done on the physiological effects of flying at high altitudes and on rapidly evolving high speeds. The new flying hospital unit started last October was, for the first time, bringing a hospital to the patient rather than the patient to the hospital. How far, he asked, had this experiment proved successful? Dr. Segal also welcomed the innovation of appointing a medical specialist to the director-generalship.

Mr. GEOFFREY DE FREITAS, under-secretary of State for air, replying to the debate, said that last year the reduction of the venereal-disease rate had been remarkable. In 1947 the figure was 22·2 per 1000, and in 1948 it was only 13·6 per 1000—a reduction of about 40%. He added that the doctors who were the links between the Institute of Aviation Medicine and the flying crews were themselves pilots. The Air Ministry thought that the teams of parachuting nurses and doctors which the R.A.F. were developing, would be very useful.

QUESTION TIME

Voluntary Hospitals' Finance

Mr. DAVID RENTON asked the Minister of Health what were the total liabilities of the voluntary hospitals other than teaching hospitals; what was the total amount of cash in hand and standing to their credit at the banks; what was the approximate total value of their tangible assets, including land, buildings, stores, and equipment on July 5, 1948; and what was the total value of the Hospital Endowments Fund at the vesting date.—Mr. BEVAN replied: The total liabilities of transferred voluntary hospitals are estimated at £14 million, of which £4,700,000 relates to teaching hospitals. Cash in hand and at the banks of the non-teaching voluntary hospitals was approximately £2½ million. The cash and bank credits of the teaching hospitals passed directly to the new boards of governors as part of their endowments and figures are not at present available. The tangible assets of transferred hospitals have not been valued nor do I consider the labour involved in carrying out a valuation would be justified. It is not yet possible to make a complete estimate of the value of the assets of the Hospital Endowments Fund but it will not be less than £18 million net.

Mr. RENTON asked the Minister what grants in aid were paid to the voluntary hospitals between the passing of the National Health Service Act and July 5, 1948.—Mr. BEVAN replied: During this period grants totalling £15,016,144 were made to 224 hospitals.

Medical Classification for National Service

Mr. GRANVILLE SHARP asked the Minister of Labour to what extent the increase in the number of men estimated as being rejected for national service during 1949 on medical ground was due to a raising of the medical standards required; and in what ways the standards were being raised.—Mr. GEORGE ISAACS replied: There has been no general raising of the medical standards, but a revised system of medical classification, known as the Pulheems system, which was introduced in June, 1948, has resulted in a more accurate assessment of a man's physical and mental fitness for service. Certain improvements in the methods of medical examination were also introduced towards the end of 1948. The effect of these changes cannot yet be fully assessed, but the latest available figures show a slight increase in the proportion of men rejected as unfit for service. Mr. SHARP: Can the Minister say what changes have been made in the medical examination?—Mr. ISAACS: There are two major changes. There is the use of mass radiography, which has made it possible to check slight cases of tuberculosis. The other change relates to the examination of ear troubles. The examination has been more intensive, not with a view to increasing the standard of fitness required, but to prevent men from being called who ought not to be called.

Mr. CECIL POOLE: Is the Minister aware that what is happening now is that men who, for instance, have defective vision in one eye, but who have all the other necessary qualifications to render good service under the National Service scheme, and who desire to render it, are being excluded, whilst those who have merely brawn and no ability are being passed into service?—Mr. ISAACS: I cannot accept that as being a statement of the position. The facts further show that at the moment the percentage of rejections is 15·9, against 13·5. This is mainly due to the innovations I have mentioned.

National Formulary Preparations and Purchase-tax

Mr. F. W. SKINNARD asked the Chancellor of the Exchequer whether he was aware that in spite of the fact that National Formulary preparations, obtained for National Health Service purposes were intended to be exempt from purchase-tax, this tax is still being levied on National Formulary 1939, and earlier preparations; and whether he would give instructions to H.M. Customs that such preparations were to be released from purchase-tax.—Sir STAFFORD CRIPPS replied: The National Formulary 1939 and earlier editions have not been approved by the Minister of Health for the purposes of the National Health Service.

Dermatitis among Fishermen

Dr. BARNETT STROSS asked the Minister of National Insurance how many cases had been notified to him of industrial dermatitis among fishermen in the North Sea, due to irritation by the sea chervil; and whether his regulations provided that those who suffered were entitled to workman's compensation whilst totally or partially incapacitated.—Mr. TOM STEELE replied: I regret that the information asked for in the first part of the question is not available. The regulations in question are widely drawn, but their interpretation is a matter for the appropriate authorities under the Industrial Injuries Act. I am not aware that any ruling has yet been given on the question whether this particular form of disease is covered or not.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

To the man in the street, doctors and the medical muddle in which we have let ourselves get involved are all a bit of a puzzle. There are some who can't understand why we don't live happily on our five or six shillings a week per potential patient, and are determined that we shall earn our money from them at any rate. Witness the Scot who told me with pride that he and his family had got their £13 worth of doctoring in the first five and a half months of the Act. Then there are others—and these include the more mathematically minded who realise that to the doctor the five or six shillings really means twopence or twopence-halfpenny—who look on us as Bevan-beaten men and women, deceived and cheated by an ungrateful country. How we manage to live they really don't know. But the majority care little for our trials. Everywhere money is tight and the extra insurance is a drain on the purse. So they prefer full pay to sick pay. After all, a Gregory powder for the stomach and goose fat for the chest have served for generations and Bevan or no Bevan the human body does not change. If one is really ill the little chemist round the corner can quickly make up a bottle, and send it round too. Doctors are best avoided. Providing they have a sufficient allocation of ink to enable them to sign the necessary certificates they can be left to their plebiscites, their regional board meetings, and their deputations to the Minister.

* * *

At tea-time in the laboratory the professor ensconced himself in his favourite chair with a stale bun and a cup of tea, and then, as was his custom, proceeded to pontificate.

"Freckles," he began, "are a sign of a sensitive constitution. Constitution is the final result of the interplay of antagonistic hormones, enzymes, and other 'humors' of the body. It is therefore a matter of balance. A well-balanced constitution is one set on so broad a base that a good knock is needed to upset it. On the other hand, a sensitive constitution, balanced, as it were, on a razor's edge, is easily upset; so in its possessor an ordinary amount of light calls up freckles; an ordinary infection with *Myco. tuberculosis* (which we all get) causes tuberculosis; and inhalation of the everyday dusts of pollen, horsehair, and so forth causes asthma. Since a constitution is by its nature psychosomatic; even smells, memories, and emotions can evoke asthma and other physical conditions, such as eczema and whip-lash bruises. That is why we often find freckles, asthma, tuberculosis, migraine, and skin affections in the same patient. You don't mean to tell me that such a person has half a dozen diseases or half a dozen diatheses.

"There are two aspects of a sensitive constitution," he continued, looking round to see if everyone was listening, "physical and mental. A sensitive constitution is a delicate constitution. Look at the delicate complexion and features and the fine hair of what the older physicians called the tuberculous diathesis. On the nervous side we have sensitivity of the eye to glare, of the ear to sound, of the skin to touch, of the nose to smell. On the mental side we have keen appreciation of colours and their shades, of the outward form of things, of music, and of beauty—artists, sculptors, musicians, poets, in fact all æsthetes. These people feel things more intensely than do their broader-balanced brethren. That is why art and insanity are near akin, and why (*pace* Harold Nicolson) so many poets have been phthisical or insane." He munched his bun loudly enough to prevent anyone interrupting, then went on: "I once knew a healthy-looking athletic boy whose parents proudly told me that he had been accepted as a cadet to train for a commission in the R.A.F. This was in peace-time, when there was keen competition for the few vacancies. 'Good Heavens,' I exclaimed, 'you don't mean he passed his medical exam?' 'Yes, why not?' 'Because of his freckles,' 'Freckles? What's that got to do with it?' 'They're a sign not only of instability of character but also of liability to tuberculosis.' Two or three years later that boy was in a sanatorium, after his country had wasted money and time in training him. If I'd been on his medical board, that would not have happened."

As the professor lent back with a self-satisfied air, the psychiatrist spoke up: "That reminds me of the worst case of freckles I ever saw. The man's face and arms (and for all I know, the rest of his body) were covered with golden freckles, like those June pastures in which you can't see the grass for buttercups. He was an inmate of a mental hospital—." "What did I say?" crowed the professor triumphantly. "Freckles and insanity; *vide supra*." "I'm afraid not," retorted the psychiatrist, "He wasn't a supersensitive bloke driven crazy by a too insistent world but a case of congenital mental hebetude—the typical village idiot—the butt of the local children."

"My tea's getting cold," mumbled the professor, "and I must buck up for my lecture."

* * *

My peripatetic colleague who delivered two after-coming heads on Westminster Bridge is not the only one to apply his knowledge of midwifery to extra-obstetrical purposes. Those of us engaged on whole-time research are often assailed by doubts as to the usefulness of much of our medical training, and we sometimes think sadly how much better it would have been if that six months we spent on our midwifery had been spent contemplating the structure of proteins. We may be wrong, though. The other day when a somewhat valuable experimental mouse was stuck in the meshes of its cage, and its fate was being bewailed by all, visions of a labour ward suddenly appeared, and by skilfully "bringing down a leg" we managed a very pretty breach delivery. We felt as pleased as we had ever done in the satisfying days on the district.

* * *

Everyone knows that the doctor's personal appearance has a potent effect on his patients. There was a student at my hospital who by merely appearing at the bedside of a woman in labour could make the pains go off; we used to put him down on our lists of the causes of uterine inertia.

Our appearance may be irremediable, but we can keep an eye on our personal habits, which may be just as important. The wrist-watch, for instance, may be a real check on a doctor's career if he uses it wrongly, for it will deprive the patient of the feeling that all our time is his (or her's). The secret is never to look at the watch when the patient can see us do it. A friend of mine saw her physician look at his wrist-watch twice during the interview. He will not see her again, which is a pity as she was one of the few private patients he had left. The cure for this habit is to buy a cheap pocket watch which one will be ashamed to look at in public.

* * *

Five of us were called to a regional hospital board committee at 2 P.M., and met punctually on the ground floor as the liftman appeared from somewhere, wiping his mouth. He took a notice down from the lift gates, and my seniors went in and up. To pass the time till the lift came back I looked at the notice, which was on an aluminium plate laid face downwards on his chair, for I was interested to see how the regional hospital board explained its employees' absence at lunch. On the metal was printed in red letters: "Closed, by Order of the Office of Works."

For some reason this annoyed me, and, as the committee was luckily a short one, I hurried to the Office of Works to inquire into this interference with hospital affairs. The official responsible, they said, had been taken ill that morning and was in hospital. They believed it was his abdomen. I went to the hospital and was told he had been in the theatre about an hour: exploratory laparotomy, porters just rung for. When I got there he was being wheeled out. It had indeed been his abdomen. On the top of the bandages was an aluminium plate, face upwards, and on the metal, painted in red letters: "Opened, by Order of the Regional Hospital Board."

(Is this true? Well; jolly nearly.)

* * *

Old lady: "I'm so thin, my doctor says I'm the most emancipated woman he's ever seen!"

Digitized by Google

Letters to the Editor

THE UNDESCENDED TESTICLE

SIR,—Surely open controversy is one of the healthiest things in medicine. Yet in your annotation of March 12 on a recent discussion at the Royal Society of Medicine you select an unimportant casual remark of mine as a "startling statement," and completely ignore my really important controversial points. These were:

1. That the classical anatomy of the region concerned is grossly inaccurate. If I am wrong, I should be confuted: if I am right, the anatomy books should be changed and all the teaching founded on bogus anatomy should be scrapped. It would be possible to settle whether I am right or wrong in one afternoon, but if there is one person harder to get into an operating-theatre than an endocrinologist it is a professor of anatomy.

2. That all workers on the subject have completely neglected diagnosis by examination. It is obvious that two quite different conditions are being lumped together: normal variations in development, and congenital deformities. The latter will no more respond to hormones than will a hare-lip.

3. That while hormone treatment claims 75% of cures, the same 75% of "undescended testicles" descend spontaneously and can be sorted out with about a 1% error by those who understand the anatomy.

4. That hormones are quite unreliable as a means of diagnosis. Often normal retractile testicles fail to take up the adult position in spite of their administration.

5. That there has been a remarkable lack of mention by endocrinologists of the dangers of hormone treatment to the cells of the testes. I have seen several testicles which I suspect to have been atrophied by this means.

6. That the classical operations are based on inaccurate anatomy and had an obvious physiological objection—that of tension on the vessels.

7. That no undescended testicle and very few ectopic ones will stay in the scrotum unless fixed. I described a method of fixing them permanently but without tension.

8. That (other things being equal) the less a surgeon knows about the subject the better his results will be, as he will operate on many normal testes.

London, W.1. DENIS BROWNE.

HEALTH CENTRES NOW?

SIR,—There are several reasons for not adopting Dr. Nicholas's suggestion of token payments for surgery attendances.

In the first place, such a practice would be wholly inconsistent with the intentions of the National Health Service.

Secondly, queues will not disappear by the elimination of trivialities as long as patients are urged to attend surgeries—even supposing that doctor and patient could ever come to agree about the exact meaning of "triviality."

Thirdly, if three hours of waiting do not constitute a deterrent, a token fee would certainly not do it either. Patients will offer payment in order to be seen out of surgery hours, and have to be refused.

Fourthly, such an expedient does not attempt to solve the problem of the doctor's wife who has to provide the staff, as well as the accommodation of the surgery. It's telephone is as essential as its sanitary facilities.

Lastly, it is a breach of courtesy (to say the least of it) to demand considerateness from the patients in inviting them to come to the surgery, and to meet this by denying them reasonable shelter and seating accommodation when they have shown themselves so considerate. If the N.H.S. is to be "safeguarded" by such pitiful neglect of common decency, it had far better not be safeguarded at all. To charge a fee on top of it is quite unthinkable.

I suggest, however, that prompt countermanding of the instructions on the new Medical Cards might be a safeguard well worth a trial. It would intimate to patients—without putting them to the trouble of a journey and a long wait—that mass attendance at surgeries is at present neither feasible nor desirable. After all, their chief incentive to bring trivialities to the surgery is the implied assurance that it is easy enough for the doctor, as long as they do the travelling and the waiting. Very few people will ask the doctor to visit if they deem the occasion to be trivial. They are poor judges on the whole, but there will never be preventive medicine unless patients are encouraged to take occasional risks with the doctor's valuable time. Only the early appearance of health centres or their prototypes will achieve what a health service means to achieve—namely, a new outlook towards disease. It is useless to preach prevention rather than cure without offering practical help in bringing the preventable to the doctor's notice in good time. At present this is not possible; but it is more important to keep the possibility in view, and to foster the demand for such a service, than to allow apathy and discouragement to doom the greatest promise which it holds, and which alone makes present hardships worth while.

My reference to a three hours' wait has misled Dr. Nicholas in an important respect—I had not ignored the doctor; I was describing a partnership where surgeries are taken in rotation, and where the patient suffered rather more than the doctor.

PRACTITIONER.

CLINICAL ESTIMATION OF BASAL METABOLIC RATE

SIR,—In his letter of March 5, Dr. Bene complains that he is unable to analyse my results because of our different interpretation of the word "correspondence." Unfortunately, in neither of his letters did Dr. Bene explain what he meant by this word. In his article (Jan. 22) he certainly did not suggest, as he now does, that his only claim for the R.P. index is to act as "an 'indicator' which indicates the direction in which the B.M.R. has shifted, and it therefore claims only an approximative correspondence with the numerical results of gas-analytical methods expressed in percentages." What he actually said in his article was that it has a "reasonable degree of correspondence to the Krogh method." He went further and claimed that this "correspondence" occurred in 67% of patients with a high B.M.R. and in 70% of others.

Let us, however, consider his new and reduced claim. If the R.P. index is to be regarded merely as an indicator of the shift of the B.M.R., one would, at least, expect that a high R.P. index would correspond with a high B.M.R. and vice versa. But what, in fact, do we find? Amongst the 100 cases quoted in my letter of Feb. 19, there are 10 instances of R.P. indices below 900, and in 9 of these the B.M.R. is higher than nought. There are 48 cases of an R.P. index above 1500; and of these, 5 have a B.M.R. below nought. In several instances the deviation is extreme. One patient, for instance, with an R.P. of 960 has a B.M.R. of + 56%; and one, with an R.P. index of 2700, has a B.M.R. of − 3%. It is of course up to Dr. Bene to claim that neither of these patients was suffering from any disorder of the thyroid gland, but I can assure him that in the first instance the diagnosis of thyrotoxicosis was confirmed histologically, and that in the second place further observation has confirmed that nothing organically was amiss. I think that here Dr. Bene has "asked for" a debating point slightly below the belt, because it is obvious that there is much less difference between a shift from + 10% to − 10% than between say + 50% and + 20%. The question of the direction in which the B.M.R. has shifted is often not very important for this reason, and I am surprised that Dr. Bene should undermine his own case by suggesting that it is.

Let us, however, leave the question of a correspondence between the B.M.R. and the R.P., partly because Dr. Bene no longer claims a correspondence and partly because he does not explain what he means by correspondence. Dr. Bene prefers the attack levelled by Dr. Martin and Miss Lovell (Feb. 12). He seeks to turn their diagram into a piece of evidence in his favour; but what, in fact, does his version of their diagram show? Merely that by changing his views about the lower limit of the normal R.P. index, which he formerly considered to be 1100 and now considers to be 900, he can show that quite a lot of patients with a normal B.M.R. have also a normal R.P. index. It would be surprising if this were not true. He would get yet another case to conform if he were to

Digitized by Google

raise the upper limit of his normal from 1500 to 1700. One is not greatly impressed by Dr. Bene's assumption that in those patients of Dr. Martin and Miss Lovell, whose B.M.R. showed the widest diversion from the R.P. index, the B.M.R.s must have been incorrectly measured or the disease incorrectly diagnosed.

But in any case, Sir, does all this matter very much? Surely the diagnosis of thyrotoxicosis remains a question of clinical acumen. The proportion of cases in which a B.M.R. is helpful in the diagnosis is comparatively small. A physician who is helped by any method which at its best is approximately correct in only two-thirds of his patients, had better leave the diagnosis of thyrotoxicosis alone.

Thyroid Clinic, New End Hospital, London, N.W.3. RAYMOND GREENE.

LYMPHOCYTES AND INTRAVASCULAR HÆMOLYSIS

SIR,—I agree with Mr. Catton (March 19) that the cells seen in peripheral blood-smears from my patient with Hodgkin's disease accompanied by hæmolytic anæmia are lymphocytes in process of dissolution; but that they are not dead cells is suggested by the normal appearance and staining reactions of their nuclei. Similar cytoplasmic protrusions are found in considerably less than 0·5% of the lymphocytes seen in smears made from normal individuals, and it is interesting that Mr. Catton has seen them in the lymphocytes of fish, in which they may occur in larger numbers than in the human subject; there may be species variations in the normal percentage of such lymphocytes.

I know of no previous description of these cells in the human subject, healthy or otherwise, and their presence in this case in greatly increased numbers seems to me consistent with the view that they are related to the intense hæmolysis observed. I am not sure that an increase in the percentage of these cells above normal limits is properly described as an "artefact," but further work including, as Mr. Catton suggests, the use of the warm-stage technique is needed for the proper evaluation of the significance of these observations.

South London Blood Supply Depot, Sutton, Surrey. R. H. TRINICK.

NATIONAL FORMULARY

SIR,—The defence of the *National Formulary* presented by some of the eminent members of the committee in your issue of March 12 is hardly necessary in view of this volume's over-all value. The truth would appear to be that one cannot be so dogmatic in a formulary as in a textbook of medical treatment reflecting the author's personal views.

I was sorry, however, to see omitted from the formulary a historical note referring to the many previous "panel" formularies and the effort which was made to embody the best in successive editions of the *National Formulary*. No doubt many of the formulas included in the present production arose originally from these sources: indeed—although I am open to correction—the formula of Whitfield's ointment at present in the *N.F.* is a modified formula suggested by my late father.

Secondly I feel that the policy regarding omission of diamorphine preparations is wrong. I believe there is a modern tendency to disregard the precise constitution of the vehicle, which is now expected to provide only a suitable way of presenting the active ingredients. Does this mean that the various preparations of heroin included in the *B.P.C.* should not be prescribed as such, the dosage of heroin being determined by altering the total dosage suitably?

The drawback about the present *National Formulary* is that the committee appear to have striven to satisfy everybody, instead of concentrating primarily on the general practitioners' requirements. Despite the reassurance that a prescriber is not bound to the formulary, in general practice it will no doubt become, as did its predecessors, the doctor's mainstay. It includes many *B.P.C.* preparations, though still lacking many of the preparations therein described, such as the syrups. It also omits the syr. cocillanæ co. of the *Drug Tariff*, although it brings in elixir caffein. iod.

Reduction of the books of reference for prescribers should be one of the ultimate aims of the committee; and when these are stabilised, such things as appliances might be reincluded although in a more comprehensive way than in previous formularies. Despite the committee's efforts such perennial troublesome formulas as mist. acid. acetylsalicyl. reappear. My late father was so disgusted with this preparation that he gave aspirin tablets with the appropriate instructions instead, and no doubt many would agree.

On reflection, studying the old *North of England Medical Formulary*, it would appear that formulation of many of the mixtures has not improved with time, and the reintroduction of some of these together with colouring agents not prone to the disadvantages of liq. azorub. might be of benefit. Despite the passage of years some of these are still prescribed.

Some of the directions given by the committee cannot be quite clearly defended. How is a doctor to prescribe ordinary syrup of figs *B.P.C.* when the committee categorically state that the compound preparation shall be dispensed? I appreciate that this is not much used, and is infrequently stocked by pharmacists; but nevertheless this is no criterion to veto its prescribing.

This is minor criticism of an outstanding effort. Finally, the value of this book would be greatly enhanced by cutting the edges of the paper according to "mixtures," &c., and by the use of tinted paper (e.g., for the children's section), to provide even quicker reference than with the comprehensive index.

Newcastle-on-Tyne. A. FORSTER.

FEMALE CIRCUMCISION IN THE SUDAN

SIR,—In your issue of March 12, Sir Basil Neven-Spence, M.P., discussed once more the question of female circumcision in the Sudan which he recently raised in the House of Commons. He has met Sudanese doctors and others, and an adequate reply was given to him on both occasions. It is difficult to see what is the purpose of his letter to your journal.

The more severe form of female circumcision, the pharaonic method, is now illegal in the Sudan. It is only natural that some time must elapse before this practice is totally abolished, especially in the more remote areas of that vast country. Rightly or wrongly the practice still has a deep-rooted significance to many of the northern Sudanese. It would create the greatest ill-feeling if action were taken to examine every girl to investigate whether or not the more severe form of circumcision was still being practised. One can remember how Regulation 33B created ill-feeling in this country, and was considered by some incompatible with the freedom of the individual. Without such dictatorial methods (which we think it wrong to enforce) accurate statistics are impossible. The facts remain that the worst form of female circumcision is now illegal, that the Sudanese themselves have formed a society to abolish this practice, and that they themselves (knowing the people) state that it is declining rapidly, especially among the more educated classes. What those educated citizens practise today will be the practice of others in time.

It has been publicly stated that the practice is spreading to the southern areas where any form of female circumcision was not previously known. One of us (J. F. E. B.) has had nearly ten years' service all over the southern Sudan, another (I. A.) has had six years' service in the Nuba Mountains. The remainder (all qualified medical men) have had from one to six years' service in the southern Sudan. We can state definitely that we have never met any case where female circumcision has been performed on one of the indigenous inhabitants of those areas. We feel that the statements made by some who have never served in those areas are untrue, and very unfair. Anyone knowing those areas and the peoples would realise that it was unlikely that female circumcision would ever be tolerated. Even if a few exceptional and isolated cases did occur, it is extremely improbable that the practice would spread so as to become a regular custom.

The difficulties are those of education, especially female education. Until all have a good primary education, and more have an intermediate education,

Digitized by Google

the practice will not be eliminated completely from some of the more remote areas. It is difficult to break the vicious circle. The operation is entirely the affair of the women. No man—not even a qualified doctor—has any part in the ceremonies at all. The husband, no matter what his feelings, is often powerless to stop the practice. By doing so, or by trying to do so, he embitters his relations with the female side of both families.

We would further point out that the Sudan now has its own elected Legislative Assembly, whose members are conscious of this problem. They are best qualified to find the most acceptable solution, and can be trusted to do so. Continued publicity, often ill-informed, might well be interpreted by the Sudanese as interference in their own affairs, and undo much good that has already been done.

A. O. ABU SHAMMA
M. A. ALI
I. ANIS
J. F. E. BLOSS
H. EL HAKIM.

c/o London School of Hygiene and Tropical Medicine, London, W.C.1.

PRACTICE OUTSIDE THE SERVICE

SIR,—If, under the little cap of darkness your peripatetics are allowed to wear, I have indeed maligned the N.H.S. I must apologise to you, to Dr. Graham, and to all within the service who find, as she does, that they have time to do unhurried work. That some doctors in the service can do this is, of course, not in dispute; that many or most at present cannot was, I supposed, generally admitted. I have not tried being a "locum" for, or a patient of, a doctor with 2500 or 3000 on his list, so I cannot give first-hand proofs; but from what has been told me by patients, by hospital residents, and by good and conscientious practitioners in the service, I cannot doubt that many doctors find they cannot give, and many patients find they cannot get, anything like the time and attention the nature of the case demands. I should be astonished if it were otherwise, and unless I am really quite wrong in my facts I think they should be freely admitted, and, indeed proclaimed, or else the defects will never be amended. If all is well with the service I and my like shall, of course, soon sink; no tears need be shed for us and perhaps no ink should be wasted on us in the meantime.

PERIPATETIC OUTSIDER.

MEDICAL TREATMENT ABROAD

SIR,—I hear that in the House of Commons Mr. Douglas Jay has been defending the Exchange Control Medical Advisory Committee against adverse criticism.[1] It may interest your readers who have had no experience of this body to know of the method by which—so far as pulmonary tuberculosis is concerned—it decides whether or not to grant currency permits.

The doctor (usually the chest physician of the area in which the applicant lives) sends the medical case-history and the latest X-ray film of the patient to the secretary of the committee; and upon this slender evidence the case for or against is judged: the opinion of the physician in charge of the case, which may be considered of the first importance since he knows the patient from long acquaintance and from every aspect, appears to carry no weight and to be ignored.

It is an axiom of medical practice, especially applicable to pulmonary tuberculosis, that no one part of the whole investigation of a case can be exalted above the rest, and that the lesser cannot be made to include the greater. Yet that is what the committee does. Without knowledge of the applicant's mental, physical, and clinical attributes it reaches—from the case-history and the shadows in an X-ray film—a decision with far-reaching effects on the sufferer. In private practice not one member of the committee would accept this evidence as sufficient to discharge his duty to the patient. One might as well expect a court of law to decide innocence or guilt without hearing both sides, and without a jury.

B. G. EDELSTON
Chest Physician, South-East Metropolitan Regional Hospital Board.

Folkestone.

1. See p. 540.

LIVER EXTRACTS

SIR,—Dr. Wilkinson, in his letter of Feb. 5 and in his Oliver-Sharpey lectures printed in your issues of Feb. 12, 19, and 26, has suggested that livers classified by the Ministry of Food as suitable for pharmaceutical purposes, are in fact diseased, lacking in anti-anæmic potency, and unsuitable for the manufacture of liver extracts. Major Guy Lloyd raised the question in Parliament on Feb. 24, when Mr. Aneurin Bevan stated that the extract, though it might not be effective, was quite safe.[1]

If it is true that the M.O.F. livers are deficient in anti-anæmic principle, it is a very serious matter and evidence should be produced in support of this contention. Although there is no statistically reliable evidence, there appears to exist a strong clinical impression that the minimum therapeutic doses of liver extract required at the present time are larger than those necessary before the war. If this is true, the fault must lie either with the patient or with the liver extract. If it is due to the extract, the fault must be either with the process or with the starting material.

At one time during the war the M.O.F. liver allocation was satisfied partly by home-killed and partly by imported liver. It was therefore possible to compare these two types of liver side by side and to compare liver extracts made from them.

There were certain differences between the imported and home-killed liver. The weight of water-soluble extractives from each was of the same order, but the amount of solid matter which accumulated in the active fraction, when a certain purification process was adopted, was higher in the case of home-killed liver. This is probably explained by a rather greater degree of autolysis in home-slaughtered material than in liver packed by one of the highly specialised stockyards in meat-exporting countries. The values of six members of the vitamin-B complex were almost identical in each type of liver. The amount of folic acid was much higher in imported liver than in home-killed. This I reported to the 1948 Pharmaceutical Conference, offering the suggestion that it could be explained by the food on the open range in the Argentine, which differed from the concentrate feeding in England.

As regards therapeutic potency, dried proteolysed liver was found to be equally effective no matter which type of liver was used for its preparation. In addition, graphs constructed from red blood-cell counts obtained during the clinical trials of parenteral extracts made from (*a*) imported liver and (*b*) liver from home-killed animals, intermingled indiscriminately when both series were drawn on the same paper.

Further evidence could be obtained by the microbiological assay of each type of liver. This is under investigation in these laboratories; but subject to confirmation we have found 2 μg. of vitamin B_{12} per g. of wet liver in the portion which on paper-chromatography migrates considerably less than riboflavin. The examination was performed after digesting liver with papain and without subjecting it to any fractionation procedure other than paper-chromatography.

The above evidence would appear to suggest that the livers issued by the M.O.F. are of satisfactory content in active material.

Dr. Wilkinson also states of certain highly purified liver preparations that it is clear that they are either "not being tested adequately before issue . . . or only some batches are being tested, or some accessory factor has been removed, or the preparation does not remain active after issue." Most reputable British manufacturers claim to test every batch. Has Dr. Wilkinson therefore taken the matter up with the manufacturers of the particular batches implicated, and preferably also with the hæmatologist who is supposed to have tested these batches? It is perhaps premature to dogmatise, but evidence appears to be accumulating that vitamin B_{12} will, so far as pernicious anæmia is concerned, entirely duplicate the effects of a parenteral liver extract; the accessory-factor hypothesis, although possible in certain cases, does not appear to stand on very firm foundation. If it is a fact that more liver is needed now than before the war, the fault may be with the patient, since for 10 years the general level of diet, especially in meat products rich in animal-protein factor, has been considerably less than that in the pre-war era.

1. See *Lancet*, March 5, p. 420.

Digitized by Google

With reference to the seasonal variation in the potency of swine-liver extracts and the apparent non-variation of extracts from calf-livers, reported by Dr. Dedichen on Feb. 26, Register et al.[2] have recently shown that the vitamin-B_{12} content of beef-muscle, as revealed by rat-growth, is considerably higher than that of pork-muscle; the vitamin-B_{12} content of pork-muscle was also found to be highly variable. They ascribe these results to the probable high degree of microbiological synthesis of active factors in the gastro-intestinal tract of ruminants and to the greater dependence of swine on exogenous vitamins. This may also explain Dr. Dedichen's observations.

With regard to dosage, most seem to advocate a dose considerably larger than the minimum necessary to elicit a maximal initial response. This view is almost universally supported by American authorities, who are not subjected to the " disabilities " of M.O.F. livers, nor to a rationed diet. The establishment of an agreed dosage scheme depends on a true standardisation of liver extracts; otherwise various authorities may be talking about entirely different doses. In this connexion it is as important to know that a given preparation does not grossly exceed its labelled strength, as it is to know that it does not fall below this point.

Under the U.S.A. system, two preparations may be allocated a unitage of 15 units and one could have many times the activity of the other. Since subsequent batches made by the same process would have the same allocated unitage without further test, the variation might be much more. The effect might be that if a maintenance dose were worked out on a patient for one batch of a particular brand, this dose might be totally inadequate for another batch of the same brand or for a second brand with the same allocated unitage.

It is evident that the answer to all questions concerned with liver extract devolves on suitable quantitative assay of potency. It is also evident that quantitative clinical assay could not be applied to every batch; so some other method will have to be employed which must be related to clinical activity. The references quoted by Dr. Dyke on Feb. 19 deal mainly with the evolution of mathematical formulæ defining the expected maximal response of pernicious-anæmia cases at various initial red-cell levels. The formulæ have been collated from a study of the records over a number of years of many cases treated with varying doses of different liver extracts. While it is true that the average response of cases receiving adequate treatment will approximate very closely to the Della Vida response prediction, there is no certainty that every case at the same initial red-cell level will give the same response to the same dose of the same liver preparation. It is also conceivable that, instead of using a formula which stipulates red-cell increase over an arbitrary period of 7 days, a more reliable criterion of satisfactory response may be obtained by superimposing a graph obtained from the test case over 14–28 days on a sheet on which has been plotted the graphed results from a number of cases at the same initial level, each treated with an adequate dose of known active material. This composite graph will show, in addition to the average response, the range of variation to expect from patient to patient. For true assay purposes, it would be essential to treat a number of cases with various doses of the same batch of liver extract, in order to find out what difference is unequivocably detectable and what degree of deviation occurs in the response of different patients to the same dose of the same extract.

Commercial liver extracts are usually tested by eliciting a maximum response (however assessed) in 2 or 3 patients with pernicious anæmia, by the administration of an arbitrary dose. For practical purposes 2 or 3 patients will satisfactorily reveal the minimum potency, but obviously the actual activity might be much higher than this. If the arbitrary test dose is greatly in excess of the minimum, various batches of the same preparation might appear to be constant in activity, although in fact considerable variation might exist. Similarly, when the test dose is truly minimal one might expect patient variability to play a large part unless a larger number of cases are used. Thus a truly constant process might appear to produce batches of varying potency.

In all assay processes the aim is to avoid such doses as would give either a full response or a very small response, and so far as I am aware, only one method of liver-extract assay using suboptimal dose schemes has been reported.

Dameshek and Castle [3] in 1934 proposed a method where a standard preparation would be injected daily for 10 days in suboptimal amounts and the reticulocyte levels determined. The test preparation was then injected into the same patient daily. If the activity in the daily dose of the sample was greater than that in the standard dose, a second reticulocyte peak was obtained. So far as I know, this method, which would be rather laborious, has not been followed up.

Among the possible non-clinical methods, there is the rat-growth method, the effect of hatchability of hens' eggs, the suppression of the effect of dried thyroid feeding on weanling female rats, and the cultivation of euglena.[4] In many of these it is almost certain that materials other than vitamin B_{12} may produce the same effect. *Lactobacillus lactis* Dorner assay of vitamin B_{12} would at present appear to offer most promise. Preliminary experiments in these laboratories have shown that it is easily possible, by the paper-chromatographic analysis, to separate the various Dorner active factors in as little as 1/200 ml. of a high-potency preparation corresponding to a good 15 *U.S.P.* unit per ml. material. It has been found that after 14 days' development with butyl alcohol, 70% of the Dorner activity of an English liver extract with total assay of 10 μg. per ml. could be recovered in the main slow-moving peak; and 50% of the activity in a 15 *U.S.P.* unit per ml. material assaying at 12 μg. per ml. could be recovered in the corresponding portion of the strip used for this preparation.

Pharmaceutical livers may be tough and they may have been derived mainly from antique cows on which time has taken its toll; but all tubercular livers and those containing abscesses are discarded at the source. It is the final material injected into the patient which matters. Given therapeutic potency and non-toxicity, the raw material might even be the dried fæces from pernicious-anæmia patients, which recent work has shown to contain 1 μg. of vitamin B_{12} per g.

The Evans Biological Institute, Runcorn. GEORGE E. SHAW.

2. Register, U. D., Lewis, U. J., Thompson, H. T., Elvehjem, C. A. *Proc. Soc. exp. Biol.* 1949, **70**, 167.

BENADRYL IN PARKINSONISM

SIR,—The history of the treatment of parkinsonism is strewn with the corpses of remedies which have fallen into disuse after an initial period of popularity. The solanaceæ alone appear to stand the test of time. This may be inevitable, but every new claim nourishes in patients and their relatives new hopes which have then to be dashed.

I have been unable to confirm the claims of Dr. Ryan and Dr. Wood (Feb. 12) on the effect of 'Benadryl' in the treatment of postencephalitic parkinsonism.

I selected 6 cases in which rigidity and speech defect were prominent symptoms. My colleagues, Dr. J. Sharkey and Dr. J. Phillips, have also treated one case each. All our patients were seen before treatment was started and after three weeks by Dr. G. A. Borthwick, medical director of the postencephalitic unit at Highlands Hospital. All the patients were given 50 mg. of benadryl three times a day and continued to take their usual dose of stramonium. In no case have we been able to register either subjective or objective improvement.

We have as yet insufficient evidence to state whether benadryl may permit a diminution in the enormous doses of stramonium which many of our patients are taking: if so, benadryl might prove a useful addition to our therapeutic armamentarium. It would appear, however, that benadryl will not produce any benefits beyond those already obtained with stramonium. High hopes in this new drug are therefore to be discouraged.

E. MONTUSCHI
Highlands Hospital, London, N.21. Assistant Physician.

3. Dameshek, W., Castle, W. B. *J. Amer. med. Ass.* 1934, **103**, 802.
4. Hutner, S. H., Provasoli, L., Stokstad, E. L. R., Hoffman, C. E., Belt, M., Franklin, A. L., Jukes, T. H. *Proc. Soc. exp. Biol.* 1949, **70**, 119.

Digitized by Google

INHALATION OF STOMACH CONTENTS

SIR,—In his interesting article of March 12, Dr. Willcox concludes that "the custom of feeding patients in labour is therefore risky and should be abandoned."

Surely it is a retrograde step to deprive a woman in labour of nourishment. Should it be necessary to anæsthetise a patient during labour, the anæsthetist should wash out the stomach contents if there is any suspicion of a full stomach. The conclusions to be drawn from Dr. Willcox's article are that only skilled anæsthetists should be employed in maternity cases, and therefore that the custom of requiring junior obstetric house-surgeons to give anæsthetics should cease.

London, S.E.13. SAMUEL LASK.

VEGANIN

SIR,—In his letter last week Mr. Warburton failed to provide evidence based on experimental investigation to show that 'Veganin' is a more effective analgesic than tab. codein. co. His reference to the rate of disintegration of these aspirin-containing tablets is as irrelevant as Dr. Macqueen's (Feb. 19).

He now implies that the aspirin, phenacetin, and codein of Veganin are in some way superior to those of tab. codein. co. This contention is sheer nonsense. Next Mr. Warburton introduces the conception of "balance of the formula." If this mysterious property is inherent in a tablet of aspirin, phenacetin, and codein bearing the trade name Veganin, on what grounds is it withheld from tab. codein. co.? The simple fact is that the attempted distinction cannot be maintained, and Mr. Warburton deserves the thanks of the profession for making this clear.

Department of Materia Medica, The University, Glasgow. STANLEY ALSTEAD.

NITROGEN MUSTARD IN BONE TUBERCULOSIS

SIR,—I have found that nitrogen mustard has remarkable powers of accelerating the resorption of exudative fluids, and of stimulating the reticulo-endothelial system and consequently the natural resistance of the body and the growth of connective and granulation tissue; it also exerts some bacteriostatic action on tubercle bacilli (Legezyński).

I use nitrogen mustard in smaller dosage than usual —i.e., 0·05–0·2 mg. per kg. of body-weight for each course of treatment. The course, usually of 3–5 injections, is repeated if necessary up to four times at intervals of two to six weeks. By this method I have avoided the major toxic reactions which usually accompany the administration of nitrogen mustard. Moreover, I do not use any nitrogen mustard that has been stored for more than six months, since such samples become more toxic.

I have given nitrogen mustard in 23 cases of tuberculosis of bone associated with cold abscesses and fistulæ, and in 8 cases complicated by total paraplegia caused by the pressure of the abscess on the spinal cord. The therapeutic effect was manifest even after the first course of treatment. The cold abscesses clearly decreased in size, and the purulent content of the fistulæ changed to serosanguineous and became much scantier. Subsequently the fistulæ healed, the fever abated, and the erythrocyte-sedimentation rate became normal.

The results were especially notable in the 8 cases of tuberculosis of the spine complicated by paraplegia. The paralytic symptoms improved remarkably within a few days of administration of nitrogen mustard, paralysis of the bladder being the first to disappear. In all 8 cases the pathological process had previously been progressive. This rapid reduction in the paralytic symptoms is in my opinion connected with the shrinkage of the cold abscess, resulting from the anti-inflammatory and resorption-accelerating actions of nitrogen mustard, which have not hitherto received sufficient attention.

In this investigation Dr. J. Kowalczk (surgeon and pathologist), Dr. R. Arend (neurologist), and Professor Legezyński and Dr. S. Slopek (bacteriologists) are collaborating.

In subsequent studies I, in association with Prof. E. Brzezicki, Dr. M. Jarema, and Dr. J. Bromowicz, of the neurological clinic of Cracow University, Prym. Dr. Horodyński, and Dr. Szyszko, have observed the marked therapeutic action of nitrogen mustard in peripheral-nerve disorders—polyneuritis, resistant syphilitic radiculitis, sciatica, and trigeminal neuralgia—where it effects a decrease in pain and paralysis.

Cracow. JULIAN ALEKSANDROWICZ.

RETROPUBIC PROSTATECTOMY

SIR,—Unlike Mr. Chapman I am not a resectionist. I reserve this operation for a minority of cases, and have had eminently satisfactory results with the retropubic operation described and practised by Mr. Millin.

I consider, however, that Mr. Chapman is right to point out, as he did in his letter last week, that in many cases prostatic obstruction is not progressive. This fact was first brought home to me whilst a resident at St. Peter's, and I have since had many opportunities of confirming what I was taught then. The presence of residual urine is the "sheet anchor" of prostatic surgery, and I feel with Mr. Chapman there is real danger that by making a plea for earlier operation in cases of prostatic obstruction, in their article of March 5, Mr. Millin and his colleagues may influence some surgeons to perform quite unnecessary prostatectomies.

St. James' Hospital, London, S.W.12. H. K. VERNON.

ARAB REFUGEES

SIR,—The Jewish Society for Human Service is concerned for the Arab refugees, victims of the fighting in the Middle East and now said to number three-quarters of a million. "Their state," wrote the *Times* correspondent in Jericho on Feb. 21, "beggars description." In particular, there is a disastrous shortage of drugs. Of the larger donations promised by governments only the British £1 million has been paid—a pound or so per head of refugees who must be fed, clothed, housed, cured. I have it on the authority of a Minister of the Crown that drugs are so short simply because food is the priority and there is not nearly enough money for everything.

May I beg your readers to send a contribution for this purpose to the Jewish Society for Human Service, 14, Henrietta Street, London, W.C.2? As the society is collecting for many other needs of these refugees contributions should be earmarked "Drugs for Arab relief."

London, W.C.2. VICTOR GOLLANCZ.

HEROIN

SIR,—Owing to the risk of addiction, it has been proposed that the use of heroin should be discontinued altogether, as in the United States.[1] That this would be a great pity will be the opinion of many who, having used the drug in common with morphine over a period of many years, have come to regard it as one of the sheet-anchors in therapy when all else has failed to produce the desired effect.

In a linctus the amount of heroin is below the dose coming under the Dangerous Drugs Acts; for intractable cough it is of great value, and one can assume that addiction is not a consideration here. For the gravely ill and the moribund heroin has many advantages over morphine. Chief of these is the absence of tendency to cause nausea and vomiting—particularly with cancer of the stomach and the rest of the alimentary tract. Both by mouth and injection it works rapidly and efficiently in much smaller doses. The exciting action mentioned in textbooks has not been observed in man, and tolerance seems to develop more slowly than with morphine. There is also much less depression; and when the two drugs are used in conjunction far less morphine is needed to relieve pain and ensure rest and sleep.

For the severe type of depression which often supervenes in the inoperable after long suffering and the administration of narcotics, a third narcotic—cocaine—is used much less often than it ought to be. The response to this addition in such cases is remarkable for the great comfort and improvement in well-being, though death is imminent. For vomiting in these conditions morphine may not be tolerated and cocaine is of great value.

One or two $^1/_{12}$-grain tablets of heroin have often been used, without habit-forming, for very ill patients who are

1. See *Lancet*, Feb. 5, p. 235.

Digitized by Google

exhausted but cannot sleep, or who are in severe pain, or very sick. They were given by mouth without divulging names and with the assurance that they could not be repeated. Such patients, having recovered, never took further interest in the matter.

Of course, mention of morphine, heroin, and cocaine on notes within the patient's reach, or verbally within his hearing, is taboo; it is surprising how slack those in attendance can be in this matter. Provided proper care is taken in keeping a careful check on heroin supplies, addiction should not occur. When it does, if heroin is not available the addict will never fail to find a substitute.

Hove. J. HARTSILVER.

HOW TO TELL THE WORLD

SIR,—Complaints of wrong reporting in your journal are usually made to preserve a reputation. Mine, alas, is to dispel your flattering assertion last week (p. 490) that I examined half a million recruits during the recent war. I clearly informed my audience during the lecture referred to that I was quoting from the *Statistical Report on the Health of the Army 1943–45*, wherein, on p. 230, is recorded the distribution of intelligence grades among the half a million recruits tested during 1943 and 1944. My own military activities during those years were quite different and many miles removed.

W. HARTSTON.

INTENSIVE TREATMENT OF SCHISTOSOMIASIS WITH SODIUM ANTIMONYLTARTRATE

SIR,—The results of intensive treatment of schistosomiasis with sodium antimonyltartrate have been reported by Alves [1] and by Alves and Blair [2] in Southern Rhodesia, and by Girgis and Aziz [3] in Egypt. Though Alves and Blair, reporting on 56 cases, had encountered only slight reactions, such as cough and vomiting, in a few cases with the two-day treatment, Girgis and Aziz, reporting on 16 cases with the two-day treatment and 9 cases with the six-day treatment, had encountered various severe toxic reactions, which were milder and less common with the six-day treatment.

Of 20 patients treated by me with a 30-hour course of sodium antimonyltartrate, 3 showed no toxic reactions, and 17 had slight headache, lassitude, and inertia. Severe reactions were seen in only 2 of these 17 patients: case 1 had phlebalgia, and case 2 had conjunctivitis and peeling of the skin of the hands (see below). Desquamation was also seen in 4 other cases, and conjunctivitis in 2 other cases. Cough developed in 9 cases, vomiting in 7, fever in 6, and erythema in 1.

CASE 1.—A healthy male, in good physical condition and weighing 158 lb., had had no history of infestation and no physical complaints, but had been exposed on numerous occasions and showed a positive cercarial antigen skin-test.[2] He was given sodium antimonyltartrate gr. 13 in seven injections spread over 30 hours. Severe phlebalgia during the second injection, followed immediately by vomiting, necessitated the splitting of the third injection of gr. $2^1/_2$ into two, one being gr. 1 and the other gr. $1^1/_2$. There was no reaction to the other injections. Five days later, contrary to advice, the patient played eighteen holes of golf without undue fatigue, and he has continued well ever since.

CASE 2.—A healthy male of average physique, weighing 142 lb., had had urinary schistosomiasis in 1937. He had been treated with sodium antimonyltartrate gr. 29 but had relapsed. He had then been treated with stibophen 35 ml. and had apparently been cured, but frequency of micturition and occasional dysuria had persisted, and for the past three years the patient had complained of general lassitude and loss of energy. The cercarial antigen skin-test was positive.

The patient was given sodium antimonyltartrate gr. 12 in 30 hours. Nausea and vomiting developed after the fourth and fifth injections, and extreme languor was a prominent feature. Three days after completion of the course a severe conjunctivitis developed and the skin of the hands began to peel. Ten days later the conjunctivitis had healed and desquamation had ceased. Since then there has been no recurrence of inertia, frequency of micturition, or dysuria.

Treatment closely followed the lines laid down by Alves and Blair. The dose of sodium antimonyltartrate was gr. 1 per 12 lb. of body-weight and was administered over 30 hours in six injections, except in case 1, where the second injection produced such severe phlebalgia that the next dose was halved, and seven injections were given in the 30 hours. In the first 6 cases each dose was diluted in 10 ml. of glucose saline, but in later cases this was superseded by an equal quantity of sterile water. No less than 5 min. was taken over each injection, the time being 10 min. with the heavier doses. All injections were given into the veins of the forearms. Linctus of codeine (*B.P.C.*) 1 fluid drachm was given half an hour before each injection to minimise the irritant effects, with notable success. The patients were admitted to hospital on the afternoon before the start of treatment and confined strictly to bed during the course of injections and for 12 hours after. They were encouraged to take large quantities of glucose, both before and during the treatment. Diet was unrestricted, a high protein intake being encouraged.

The following case is typical of the results achieved with this treatment:

CASE 3.—A healthy male, aged 28 and weighing 154 lb., had had urinary schistosomiasis in 1932 and been treated with intravenous sodium antimonyltartrate gr. 29. Since then he had not been exposed to infestation, but during the past two months he had lost 1 st. in weight and had felt weak and listless. On examination the liver was palpable two finger-breadths below the costal margin, and ova of *Schistosoma mansoni* were found in the stools. Nothing else abnormal was detected. Sodium antimonyltartrate gr. 13 was given in six injections of gr. 2, 2, $2^1/_2$, 2, 2, and $2^1/_2$ without toxic reactions. Fourteen days later the liver edge was only just palpable and the patient was feeling fit and well. Six months later he had recovered his lost weight and was feeling extremely well; nine successive specimens of stools showed no ova, and sigmoidoscopy was negative.

In 10 cases in which ova had been observed in the stools or in the urine no ova were found six months after the completion of treatment. No ova were found in 2 of these cases eight months, and in another 2 nine months, after treatment. In all cases nine successive specimens were examined. These findings are no proof that the intensive treatment can always cure, but they are in harmony with the results obtained by Alves and Blair.[2] At no time were any of the toxic reactions pronounced, and none of the more serious—e.g., jaundice, hæmorrhages, and cardiac failure—were noted. All these minor symptoms speedily and spontaneously disappeared within fourteen days, leaving behind a feeling of well-being, which many of the patients had not experienced for some years. It therefore seems that the toxic effects are not so severe as might have been expected, and by no means so severe as has been feared by many whose knowledge of the toxicity of sodium antimonyltartrate has led them to view the "fast antimony" treatment with misgivings.

Gatooma, Southern Rhodesia. G. A. RAIL.

1. Alves, W. *S. Afr. med. J.* 1945, **19**, 171.
2. Alves, W., Blair, D. M. *Lancet*, 1946, i, 9.
3. Girgis, B., Aziz, S. *Ibid*, 1948, i, 206.

STERILISATION OF POLYTHENE TUBING

SIR,—The technique of replacement transfusion of babies requires the use of 'Polythene' tubing which is somewhat delicate. Because polythene will not stand temperatures above 110°C, the methods of sterilisation used by many are either boiling for 15 minutes immediately before use, or storage in 1% cetrimide. As these methods are considered unsatisfactory on several counts, alternative techniques have been tried. Of these I can recommend the following method, which we have adopted in this department.

1. 12-in. lengths of 9 mm. glass tubing are wool-plugged and sterilised in the hot-air oven (160°C for one hour).

2. Two 9 in. lengths of polythene tubing are loaded into each sterile glass tube.

3. The tubes are then sterilised by steaming for 30 min. on three consecutive days.

In the process of steaming the catheter shrinks in length, but remains perfectly flexible.

Digitized by Google

The main advantages of this technique are that the polythene tubing is heated in straight tubes, and so does not curl; that the sterile tubes can be stored easily, and are dry, and ready for immediate use.

Bernhard Baron Research Laboratories, Queen Charlotte's Maternity Hospital, London, W.6. JOHN MURRAY.

Public Health

Infant Vaccination

IN the last half of 1948 the proportion of infants in Manchester successfully vaccinated against smallpox was less than half the proportion in the first six months. This is revealed in a memorandum to the city health department by Dr. C. Metcalfe Brown, the medical officer of health. The percentage of infants vaccinated fell from 72·90 for the period from Jan. 1 to July 4, to 30·34 for the remainder of the year. (These percentages are based on uncorrected figures.)

In November and December a sample survey of the attitude of parents of children aged 4–6 months gave the following results:

Vaccination not desired	278
Doubt about vaccination	669
Vaccination desired	1312
	2259

During this period only 599 completed vaccinations were reported. Dr. Metcalfe Brown points out that the decline in vaccinations is in no way attributable to the attitude of parents, which has not changed. The reasons for the decline, he says, appear to be:

1. That whereas previously most vaccinations were carried out in the homes by the public vaccinators, medical practitioners, under heavy pressure of work, now expect most mothers to bring their infants to the surgery. This may entail three or more visits, and some parents are reluctant to take infants into surgeries crowded with sick people.

2. That while many doctors are coöperating wholeheartedly in the scheme, some would be more enthusiastic if agreement were reached with regard to vaccination fees. Some may never be active in relation to vaccination, through lack of conviction or pressure of work.

Dr. Metcalfe Brown believes that, even to attain the former level of immunity, supplementary measures will be needed. Under the Act, Manchester has proposed, and the Ministry of Health and the local executive council have approved, that, if necessary, vaccination sessions should be held at welfare and other centres, and at the health-department offices. He recommends that vaccination should be available at infant-welfare centres, either in the course of ordinary sessions or at special sessions; but, emphasising the need for close collaboration between general practitioners and the health department, he also recommends that local representatives of the profession should first be consulted.

Births and Marriages in 1946

A review by the Registrar-General,[1] published this week, shows that in 1946 there was a rise in the birth-rate, a considerable fall in illegitimacy, and a fall in the proportion of stillbirths.

Births.—There were 820,719 live births, which represented a birth-rate of 19·2 per 1000 total population. This was an increase of 3·3 per 1000 over the rate in the previous year and was the highest since 1923 when it was 19·7. Later figures show that the birth-rate further increased to 20·5 in 1947 but fell considerably in 1948, the provisional rate for that year being 17·9. In 1946 there were 53,919 illegitimate live births—6·6% of the total, compared with 9·3% in the previous year. This proportion fell to 5·3% in 1947. Still-births numbered 22,915, representing a rate of 27 per 1000 live and still births, compared with 28 in the previous year. By 1948 this rate had fallen to 23.

Marriages.—In 1946 these numbered 385,606, which, though less than in the previous year, was still substantially higher than the pre-war average. In 1947, however, the number again rose, being 399,936 (provisional). The marriage-rate in 1946 was 18 per 1000 total population, compared with the average rate for the previous ten years of 17·9.

Fertility.—Of the legitimate maternities 44·9% were to mothers with no surviving previous children, 30·2% to mothers with one surviving child, and 12·9% to mothers with two surviving children. There were 10,788 maternities resulting in multiple births, of which 85 were triplets.

1. Registrar-General's Statistical Review of England and Wales, Tables, Part II (Civil), 1946. H.M. Stationery Office. Pp. 148. 2s. 6d.

Influenza

During the week ended March 21 there were 321 deaths from influenza in the great towns of England and Wales, compared with 259 in the previous week. Deaths remained practically the same in London and the south-east, but there was a rise in the north and in the midlands; it may be that some of the increase was due to the cold weather. Incidence has been high in certain places—e.g., Salford, the West Riding of Yorkshire, and Birmingham—but the disease has been mild. From one London borough a report has been received that four patients suffering from influenza developed coffee-ground vomiting and melæna.

Nearly all the isolations of virus have been of virus A, but virus B has been isolated from material received from two school outbreaks and from a fatal case of staphylococcal pneumonia at Leicester.

Whale-meat Regulations

Under the Food and Drugs (Whalemeat) Regulations, 1949, which came into force on March 20, the importation of whale-meat and whale-meat products into England and Wales for sale for human consumption, is prohibited unless accompanied by a "veterinary certificate," certifying that the meat has been inspected and satisfies criteria laid down by the Ministry of Food. The regulations also include provisions against contamination of whale-meat in shops and on stalls, during transport, and from handling in wholesale markets, cold stores, and elsewhere.

Diary of the Week

MARCH 27 TO APRIL 2

Monday, 28th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Mr. R. J. Last: The Knee-joint. (Arnott demonstration.)
5 P.M. Mr. David Band: Neurological Disorders of the Urinary Bladder.

WESTMINSTER MEDICAL SCHOOL, Horseferry Road, S.W.1
5.30 P.M. (Meyerstein lecture theatre.) Clinico-pathological demonstration on Steatorrhœa in Childhood.

Tuesday, 29th

ROYAL COLLEGE OF SURGEONS
5 P.M. Prof. A. Franceschetti (Geneva): Cataract Associated with Lesions of the Skin.
6.15 P.M. Prof. G. B. Bietta (Pavia): Ophthalmic Aspects of Protein Deficiency and Disordered Protein Metabolism.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

Wednesday, 30th

ROYAL COLLEGE OF SURGEONS
5 P.M. Dr. E. Hartmann (Paris): Psychosomatic Symptoms in Ophthalmology.
6.15 P.M. Prof. H. J. M. Weve (Utrecht): Ophthalmic Manifestations of Besnier-Boeck's Disease.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
10 A.M. Mr. A. C. Deverell, F.D.S.R.C.S.: Relationship of Dental Disease to Diseases of the Throat, Nose, and Ear.

Thursday, 31st

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. Charles Gray: Surgical Treatment of the Painful Hip-joint. (Hunterian lecture.)

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM
9.45 A.M. (1, Wimpole Street, W.1.) Opening of annual congress.

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. H. Gordon: Pitfalls in Treatment.

Friday, 1st

MEDICAL SOCIETY FOR THE CARE OF THE ELDERLY
2 P.M. (Belmont Road Hospital, Liverpool.) Lord Amulree: Viewpoint on Geriatrics. Dr. Marjory Warren: Overcoming Physical Limitations.

Saturday, 2nd

MEDICAL SOCIETY FOR THE CARE OF THE ELDERLY
9.30 A.M. Dr. J. W. Affleck: Personality Factors in Senile Psychosis.

Digitized by Google

Obituary

KAROLINA WIDERSTRÖM

MED. DR.

The death is announced of Dr. K. Widerström, Sweden's pioneer woman general practitioner. Born in 1856, she first qualified from the Royal Central Institute as a physiotherapist. Later she took up medicine, and after completing her studies she became an assistant physician in the gynæcological department of the Sabbatsberg Hospital in Stockholm. In 1889 she started her own practice in that city. In due course she was appointed a member of government committees on education, and women's professional education. A good lecturer, she travelled all over the country to speak on personal hygiene and public health. For many years, she was also a member of the Stockholm city council. "She held progressive views," writes a correspondent, "but her criticism was sound and well-balanced, her proposals and plans practical. A woman of strong personality, she brought an independent mind and broad vision to bear on the social and educational questions of her day. She gained the respect and the confidence of her patients and colleagues, and the esteem of the authorities and the public."

Births, Marriages, and Deaths

BIRTHS

CONNELL.—On March 14, the wife of Dr. Michael Connell—a daughter.
EAGER.—On March 16, at Burford, Oxon, the wife of Dr. R. G. Eager—a son.
GILBEY.—On March 16, at Durban, the wife of Dr. A. L. Gilbey—a daughter.
GORDON.—On March 15, at Walton-on-Thames, the wife of Surgeon Lieut.-Commander K. G. O. Gordon, R.N.—a son.
HALL.—On March 13, at Mwanza, Tanganyika, the wife of Dr. Christopher Hall—a daughter.
KINGSTON.—On March 13, the wife of Dr. John Kingston—a son.
MACKENZIE.—On March 12, at Shrewsbury, the wife of Dr. G. K. Mackenzie—a daughter.
MARTIN.—On March 12, at Cambridge, the wife of Dr. Laurence Martin—a daughter.
NEWSHOLME.—On March 11, at Emsworth, Hants, the wife of Dr. A. D. Newsholme—a daughter.
PAKENHAM-WALSH.—On March 14, at Lancaster, the wife of Dr. R. Pakenham-Walsh—a son.
PAYNE.—On March 14, in Birmingham, the wife of Dr. John Payne—a son.
STEPHENS.—On March 13, in London, the wife of Dr. Hugo Stephens—a son.
TRUST.—On March 1 in London, the wife of Dr. Desmond Trust—a daughter.

MARRIAGES

BELL—THOMAS.—On March 12, in London, Raymond Bell, M.B., to Lena Thomas.
RYCROFT—BUTTERFIELD.—On Feb. 10, at Heathfield, Sussex, John Alan Rycroft, M.B., to Catherine Butterfield.

DEATHS

ATKINSON.—On March 12, at Northampton, Edward William Atkinson, M.R.C.S., aged 67.
BATES.—On March 18, at Sandwich, Kent, John Edwin Bates, T.D., B.A., M.B. Camb., aged 79.
BROWN.—On March 13, at Cranleigh, Daniel Dorward Brown, M.D. Durh., aged 83.
BRUCE.—On March 14, at Woburn, Beds, Robert Tennant Bruce, M.D. Edin., aged 76.
BULSTRODE.—On March 18, at Chichester, Christopher Victor Bulstrode, D.S.O., M.A., M.D. Camb.
CONNER.—On March 16, at Greenford, John Richard Tarrant Conner, B.A., M.D. R.U.I.
COOPER.—On March 13, at Salcombe, Charles Edward Cooper, B.A., M.B. Camb.
CRAWFORD.—On March 14, John Martin Maynard Crawford, O.B.E., F.R.C.S.I., lieut.-colonel, R.A.M.C. retd.
GRINLING.—On March 14, at Sheffield, Philip Newman Grinling, M.B. Durh., aged 41.
JOHNSON.—On March 15, at Heswall, Cheshire, William Johnson, M.C., M.D. Lond., F.R.C.P.
MACLAREN.—On March 17, Henry Colin MacLaren, M.A., M.B. Camb., D.A., aged 37.
PRICE.—On March 17, Clifford Price, M.R.C.S.
STEWART.—On March 14, Howard Douglas Stewart, L.R.C.P.E.
STOKER.—On March 21, in London, George Morris Stoker, M.R.C.S., aged 50.
WADHAM.—On March 14, at Ryde, I.o.W., Frank Jesser Wadham, M.R.C.S.
WHITTING.—On March 17, at Lyme Regis, Robert Everard Whitting, M.C., M.A., M.D. Camb.
YORKE-DAVIES.—On March 11, at Nakuru, Kenya, John Wynne York-Davies, M.R.C.S.

Notes and News

SENIOR HOSPITAL MEDICAL OFFICERS

A Ministry of Health letter to regional hospital boards observes that some of the phraseology relating to senior hospital medical officers used in the proposed terms and conditions of service [1] appears to have caused misunderstanding about the kinds of officers regarded as falling into that group. The Ministry has therefore drawn up the following notes to clarify the position.

1. The first group—i.e., those described in the proposed terms as "specialists"—is intended to include only those members of medical and dental staffs who are regarded as of full consultant and specialist status, whether as a result of assessment by a review committee (in the case of existing staff) or of selection by an advisory appointments committee (in the case of future staff appointments).

2. The group described in the proposed terms as "senior hospital medical officers" is intended to include members of medical staffs performing clinical duties whether of a general or special nature; that is, it includes officers who may be engaged (whether wholly or partly) in a special branch of medicine—e.g., anæsthetists, pathologists, tuberculosis officers, venereologists, psychiatrists, and more rarely physicians, surgeons, or obstetricians—but who individually are not regarded as of full consultant and specialist status. In this sense, therefore, the heading "Other *Non-Specialist* Grades" in the proposed terms, is inaccurate and should be amended by omitting "Non-Specialist."

PROGRESS IN MENTAL HEALTH

THE public is hardly yet informed of the steady and constructive work done by the National Association for Mental Health—work seriously hampered by lack of funds.

The training school for *mentally defective children* under 16, at St. Leonards, has been full all the year and is now approved under the Mental Deficiency Act, which means that the regional hospital board can maintain the occupants just as the local authorities used to do. The lease of a home for low-grade mental defectives at Basingstoke is now about to run out, and the home will probably be taken over by the South-West Metropolitan Regional Hospital Board, though the association will continue to have a small interest in its management.

A new *convalescent home for epileptics* has been opened at Fairwarp, Sussex; it takes 9 men and women, and is reserved for those recovering from illness who are debarred from ordinary convalescent homes because of epilepsy. King Edward's Hospital Fund for London contributed £800 to the cost of equipment, and during the first summer 90 patients were entertained there. Applications came from all over the country, and the need for such homes is evidently so great that the association hope, with the aid of the King's Fund, to open at least one more.

There are now eleven *agricultural hostels* for mentally defective men—in Gloucestershire, Yorkshire, Hampshire, and Shropshire—housing some 360 landworkers. The men are guaranteed full employment by the county agricultural executive committee. Of 870 who have passed through the hostels in six years many have shown a gain in initiative and sense of responsibility, and 97 have been discharged from certificate under the Mental Deficiency Act; a further 75 are on licence to farmers and hope to gain their discharge. Some 80 men each year prove unsuitable for the work (mainly because they cannot stand the physical strain) and have to be returned to their institutions. The association hope that the regional hospital boards will take up the plan on a bigger scale.

A parallel scheme to open a hostel for epileptic men has so far failed, the prejudice against epileptics still being too great. This seems to offer another opportunity for public education: professional opinion about epilepsy has changed greatly in recent years, and it is time the public was helped to a better understanding of the epileptic and his capacities. The association, in coöperation with the Home Office, hope soon to open two approved schools—one for girls and one for boys.

Besides supporting these heavy undertakings, the association publish pamphlets and posters, and the quarterly journal,

1. See *Lancet*, March 19, p. 491.

Digitized by Google

Mental Health. They also arrange lecture courses, and encourage the formation of local associations. They run an important social-services department which employs 22 psychiatric social workers, and 59 other social workers. These relatively few workers visit and help patients in their homes; in 1947–48 they dealt with 12,707 cases, of which over 5000 were new.

This great body of work is undertaken on the slenderest funds. The association has some fixed assets, such as the freehold of certain homes and the furniture and equipment of homes and offices, but its sole cash reserve is £3700. With the backing of some large trust fund, such as the Red Cross Society or the Nuffield Foundation, it could do much more, and even better, work; and with adequate public support it could extend its scope to relieve every sort of personal difficulty facing the mentally ill. Those with funds to allocate should think whether this is not a more urgent need than some on which they lavish donations.

PARLIAMENTARY FOOTNOTE

WHEN he cut the first sod of the site of the Woodberry Down health centre at Stoke Newington on March 16, Mr. Aneurin Bevan returned to the plea which he had made earlier in the House of Commons that, as there were no statutory limitations to what the health service could do, the Bill for analgesia in childbirth was unnecessary. "I do most earnestly beg and pray," he added (*Times*, March 17), "that in this field, where emotions are so bound up with our ordinary human feelings, where human pain is the thing we are trying to relieve, that no attempts will be made to offer to anybody in pain the hope of relief when the physical capacity of relief may not be obtainable. It is also undesirable that we should suggest that this or that group of sufferers should have claim against another group of sufferers."

ANXIETIES OF MARRIED PEOPLE

MANY marriages are handicapped at the start by sexual difficulties between the partners. Discussing some of these at a conference arranged by the Family Planning Association, held in London on March 12, Dr. Noel Harris said that the common causes of impotence seen among men attending his clinic were failure of erection, premature ejaculation, and lack of sexual desire. Premature ejaculation, being commonly associated with ignorance and consequent anxiety, can often be dealt with in a single session by giving the man adequate instruction and reassuring him. Failure of erection may be due to constitutional causes, and, if so, little can be done about it. If the origin is psychological the patient will need a long intensive course of psychotherapy, and the same is generally true of lack of sexual desire. Frigidity and dispareunia in women may also spring from anxiety, from lack of sexual experience, or from fear associated with some unfortunate experience. The woman, may be alarmed by her husband's approach. Her half-voiced doubt that his roughness may be a sign of perversion can be set at rest by explaining to her that perversion is a state in which intercourse is *replaced* by some other act; and her apprehension can often be eased by reminding her that the male desire to capture, and the female desire to be subdued, are normal, and to be found among birds and animals as well as among mankind.

On the subject of homosexuality Dr. Harris noted that sexual behaviour depends on many factors—endocrine, constitutional, and psychogenic. Patterns of behaviour range from complete heterosexuality to complete (biologically determined) homosexuality, with every grade of bisexuality between. There is much evidence of bisexuality throughout the animal kingdom, and all animals show homosexual behaviour. The bisexual person may be swung towards homosexuality by incorrect upbringing; and is therefore not blameworthy. A patient in seeking advice about homosexual tendencies is usually suffering severely from guilt feelings; and the first duty of the doctor is to reassure him, and to explain that the form of his sexual desires is not within his control. On the other hand, the same moral rules hold for him as for the heterosexual person: if he seduces others or behaves indecently he may be punished, and rightly. Once his acute anxiety has been allayed the compulsion he often feels towards these antisocial acts will very likely disappear, and he becomes able to control his behaviour if not his desires.

Speaking of the frigid woman, Dr. Joan Malleson remarked on the power of the taboos of early childhood to inhibit the behaviour of the grown person. Some women only need a little instruction to overcome their difficulties to achieve orgasm; and others can avoid much of the frustration which frigidity induces. Dr. Malleson thinks that a woman should never be told her frigidity is due to her husband's lack of technique. A man is none the better for being made to feel inferior, nor does it help his wife to believe him so. She had far better feel the fault lies with her: though there are, in fact, no faults—only difficulties.

DOSTOÏEVSKY'S ILLNESS

RUSSIAN novelists often lead their readers to suppose that the chief occupation of Russian university students, apart from their revolutionary activities, was to cough, spit blood, and die either of tuberculosis or suicide. Dostoïevsky's novels are freely peopled with tuberculous characters, and Dr. Silveira[1] now gives us thumbnail sketches of them, with tentative diagnoses of the stage of pulmonary tuberculosis reached by each. He then goes on to marshal the evidence suggesting that Dostoïevsky was himself tuberculous—as well as epileptic. His mother was tuberculous and died young, and his nurse died of chest disease—two important sources of infection for the child—and against paternal orders he associated with the diseased paupers in his father's infirmary. At the age of about 17 he lost his voice for a time, and when it came back it was permanently altered; Silveira suggests that this was tuberculous laryngitis, though hysterical aphonia can produce the same effect. Dostoïevsky became an army officer, and at the age of about 25 underwent medical treatment for a condition characterised by cough, swollen cervical glands, a hoarse voice, and a cadaveric complexion. He was then exiled to Siberia for four years, and on his return he lived a life of poverty with his mistress, a young tuberculous woman, Maria Issaiev (the original of the widow Ivanovna in *Crime and Punishment*), who died of tuberculosis—yet another source of reinfection. A discussion follows of Dostoïevsky's bronchiectasis which developed during his wanderings in Europe after Maria's death. Finally, at the age of 60, he died of a series of hæmoptyses in a couple of days. Q.E.D.

ELECTROTHERAPY

A MEETING of the Heberden Society in London on March 4, with Dr. W. S. C. Copeman in the chair, was devoted to the question Is Electrotherapy Empirical? Mr. C. W. Marshall, speaking as an electrical engineer, contrasted German and English practice in the use of ultraviolet light as an example of the antiquated and empirical use of physical methods in England. He was highly critical of the numerous eponymic "currents" and said that all electricity used could be described in terms of linear and exponential functions. Although English school textbooks on electricity were good, the less said about English medical electricity textbooks the better. Dr. P. Bauwens agreed with some of Mr. Marshall's criticisms, but by no means all. We knew a good deal, he said, about the action of direct and high-frequency and low-frequency alternating currents: he saw no reason why the term "galvanic stimulation" should not be used by the doctor in the same way as "galvanised iron" is used by the engineer. Equipment was in many places crude, through lack of money, but it did its job. Measurements of the current were usually adequate, but some workers needed the coöperation of electrical engineers—e.g., in the measurement of tissue temperature in a high-frequency field.

University of Cambridge

On March 12 the following degrees were conferred:

M.D.—S. F. L. Dahne.

M.B., B. Chir.—Norman Allsup,* William Beautyman,* A. E. Neill. * By proxy.

University of Manchester

On May 18 the honorary degree of LL.D. is to be conferred on the Very Rev. Garfield Hodder Williams, M.B., dean of Manchester from 1931 to 1948, and of D.SC. on Dr. A. E. Barclay and Miss Katherine Coward.

Mr. A. W. G. Ewing, PH.D., at present reader in the education of the deaf, has been appointed Ellis Llwyd Jones professor of the education of the deaf and director of the department.

---

1. A Tuberculose na Vida e na Obra de Dostoïevsky. By HOMERO SILVEIRA, technical assistant in the State tuberculosis department, São Paulo. Rio de Janeiro: Pongetti. 1948. Pp. 61.

Digitized by Google

University of Durham

Dr. E. A. Pask has been appointed to a professorship of anæsthetics at King's College, Newcastle-on-Tyne, personal to himself. Dr. Pask has held the readership in anæsthetics since 1947.

University of Leeds

Dr. R. J. Still has been appointed university medical officer.

Dr. Still was educated at Leeds Grammar School, at Magdalene College, Cambridge, and at Leeds University, graduating B.CHIR. in 1934. He has held hospital appointments in this country, and was medical officer and medical superintendent of the Foster Hospital, Shantung. For two years he was in charge of a Japanese camp for civilian internees in Shanghai, and afterwards he became hospital superintendent at the Cheeloo University medical school.

University of Aberdeen

Dr. W. Malcolm Millar has been appointed to the chair of mental health in succession to Dr. D. R. MacCalman who is now Nuffield professor of psychiatry at Leeds.

Dr. Millar, who was born at Perth 35 years ago, was educated at George Heriot's School and the University of Edinburgh, where he graduated M.B. in 1936, taking his M.D. with high commendation three years later. In the same year he also took the diploma in psychology. After holding house-appointments at the Deaconess Hospital in Edinburgh he joined the staff of the Royal Edinburgh Hospital for Mental Diseases. During the war he served in the R.A.M.C. with the rank of major, chiefly on War Office selection boards. In 1946 he was appointed lecturer in mental health in the University of Aberdeen and assistant physician at the Royal Infirmary. His published work includes papers on remissions in schizophrenia and on air-raid noises and psychotherapy.

Pædiatric Congress

The Sixth International Congress of Pædiatrics will be held in Zurich during the last ten days of July, 1950. Further information may be had from the secretary-general, Prof. Emmett Holt, Bellevue Hospital, New York 16, N.Y., or the president of the congress, Prof. G. Fanconi, Kinderspital, Zurich.

Liverpool Regional Hospital Board

At their meeting on March 3 the board were informed of the decision of the Ministry of Health that their estimate of £7,147,956 for revenue expenditure in 1949–50 must be reduced by £510,000. Also the estimate of £597,282 for capital expenditure must be reduced by £263,282. The board decided to hold a special meeting to consider these reductions.

Four of the five Liverpool hospital management committees have agreed to work together and to form a joint contracts committee for hospital supplies. These four groups have 24 hospitals and clinics containing 5250 beds. This organisation will be parallel to the joint finance committee, which will act in regard to all financial matters affecting the same four hospital management committees.

Health Centres

London County Council this week considered a proposal to construct a health centre as part of the architectural exhibition which is to be prepared for the Festival of Britain, 1951. This exhibition will consist of a specimen neighbourhood unit in the Poplar and Stepney reconstruction area. The proposed centre, in East India Dock Road, will serve immediately some 30,000 and ultimately about 18,000 people. The design will be on the lines of the centre under construction at Woodberry Down.

Hertfordshire County Council have submitted to the Ministry plans for a centre to serve Oxhey and Carpenders Park. This district has a growing population, which is expected to number 18,720 by the middle of 1951. There will be accommodation for 8 doctors, with a waiting-room, an examination room, and a secretary's room adjacent to each consulting-room; a minor surgical unit; an isolation room; and an ophthalmic room and dark room. Rooms will be available for a nursing and home-helps office and a nurses' duty room. Provision will also be made for five dental surgeries, a maternity and child-welfare clinic, and a school health clinic. Since pharmacists' shops are to be incorporated in the new district, a pharmaceutical service will not be offered at the centre. The regional hospital board, who point out that the centre is close to Watford with its hospital resources, have asked only for a room which their consultants might use when necessary; and the general practitioners have agreed that a surgery can be used for this purpose.

National Marriage Guidance Council

The council is holding a conference at the Esplanade Hotel, Scarborough, from May 14 to 21. Further information may be had from the secretary, 78, Duke Street, London, W.1.

Dawson Williams Memorial Prize

As no awards have been made since before the war, the trustees have this year awarded two prizes, each of 60 guineas. Prof. J. C. Spence receives one "for his research into diseases of children"; Prof. A. A. Moncrieff the second "for his work for child health."

Faculty of Anæsthetists

The faculty's first anniversary was marked by a dinner at the Royal College of Surgeons on March 16, when Mr. A. D. Marston, the dean, spoke with gratitude of Lord Webb-Johnson's assistance in founding this organisation. Fellows and members would, he said, do all they could for the college. They were proud of the way the college had turned itself into a lively centre of postgraduate education; and through its close association with the college the faculty would avoid the dangers of isolation that threatened the specialties. Lord Webb-Johnson, F.R.C.S., who replied for the college, found it hard to imagine an anæsthetist working in isolation; and he underlined the growing importance of the anæsthetist as what had been termed the "clinical physiologist" to the surgical unit. As a surgeon Mr. V. Zachary Cope, who proposed The Faculty, welcomed the chance of saying exactly what he thought of anæsthetists; and the explanation of his sentiments, in verse, was well received. In his response, Dr. Bernard R. M. Johnson referred to the vast amount of work done by Mr. Marston towards setting the faculty on its feet. Mr. D. W. Logan, D.PHIL., and Sir Cecil Wakeley spoke for The Guests, in response to a toast proposed by Dr. Frankis T. Evans.

Prof. E. C. Dodds, F.R.S., and Dr. Peter Bishop are visiting Barcelona, under the auspices of the British Council, to take part in a course on endocrinology arranged by the medical faculty of the university.

Mr. G. L. Keynes has been appointed a member of the advisory committee on the administration of the Cruelty to Animals Act, 1876, in place of Sir Gordon Gordon-Taylor, who has resigned.

Mr. St. John Buxton is visiting Greece, on behalf of the British Council and the British Medical Association, to lecture on orthopædics, amputations, and gunshot wounds.

CORRIGENDUM: *Systolic Murmurs*.—The penultimate sentence of the first paragraph of this annotation last week (p. 489) should read: "Where there is any question of the supposed murmur being actually a split heart-sound, doubt may be resolved by a phonocardiogram."

Appointments

HOWARD, R. C., M.B. Camb., F.R.C.S.E.: asst. orthopædic surgeon, Norfolk and Norwich Hospital.
KIMBELL, N. K. B., M.B. N.Z., M.R.C.O.G.: specialist obstetrician, Peterborough and District Memorial Hospital.
SHEEHAN, SHEILA, M.D., B.SC. Dubl., M.R.C.P.: registrar, neurological department, medical school, University of Sheffield.

Fulham Hospital:
MEHLMANN, SAMUEL, MED.DIP. Lwow: junior anæsthetics registrar.
WAKELIN, J. L., M.R.C.S., D.L.O.: part-time senior registrar to ear, nose, and throat department.

London County Council Public Health Department:
Asst. M.O.H.:
KNOWLSON, MADELINE, M.R.C.S.
MCKEIGUE, VALERIE, M.B. Lond.
RICHARDS, HILDA, M.R.C.S.

Colonial Service:
DELANY, L. F. B., M.B. N.U.I.: M.O., Tanganyika.
EATON, R. D. P., M.B. Manc.: M.O., Sierra Leone.
GORDON, I. H., M.R.C.S.: pathologist, Nigeria.
MCKINLEY, D., M.R.C.S.: M.O., Sierra Leone.
PAYNE, B. A., M.R.C.S.: M.O., Nyasaland.
RAINSFORD, C. R. C., M.D. Belf., D.T.M.: senior M.O. in charge, Zanzibar.
ROBSON, T. W., M.R.C.S.: M.O., Tanganyika.
STILL, R. M. L., M.R.C.S.: medical superintendent, Mental Hospital, Barbadoes.
WILLIAMS, A. W., M.A., M.D. Camb., M.R.C.P., D.T.M. & H.: medical superintendent, Mulago Hospital, Uganda.

Digitized by Google

HISTORICAL BUILDING
DES MOINES, IOWA

THE RÔLE AND VALUE OF THE ANAMNESIS *

SIR ADOLPHE ABRAHAMS
O.B.E., M.A., M.D. Camb., F.R.C.P.
CONSULTING PHYSICIAN TO WESTMINSTER HOSPITAL

"A major distinction between good and bad doctors is the time devoted to history-taking and the ability to interpret a history. Far more mistakes are made by putting too much significance on doubtful physical signs and neglecting the clear indications of the history than by the opposite process."—Prof. Robert Platt, *Lancet*, 1947, ii, 305.

ALTHOUGH, as I shall subsequently elaborate, I do not share to the full the estimation accorded to the importance of the anamnesis and the advocacy with which its claims are advanced, I can certainly share with all teachers an appreciation of its significance not merely in a student's education but also as a routine procedure throughout our professional life, and no apology is needed for the selection of my subject as eminently suitable for this occasion.

It is inevitable, if admittedly platitudinous, to deplore, on the *laudator temporis acti* principle, the ever-increasing tendency to neglect the fundamental approach to the patient. Our predecessors insisted upon the most painstaking clinical application preceded by a scrupulous attention to the history. The student of today exhibits an insatiable appetite for laboratory investigations and other adventitious aids to diagnosis. This practice is a reflection of present-day hustle, the desire for a convenient and a relatively congenial short cut, to which some sympathy must be conceded when one contrasts the modern tempo with the dignified leisureliness of the past, even the comparatively recent past of those of us who now rank as seniors.

As a routine procedure, taking a history is a time-consuming unalluring obligation. It demands unlimited patience in consequence of the familiar handicaps imposed by nervousness, deafness, stammering, peculiarities of articulation, and an inability to describe or explain.

To these must be added the difficulty of securing the patient's confidence even if he is otherwise well equipped to coöperate. We may call this the art of medicine in distinction from the science. Most of us succeed fairly satisfactorily with the science; if we are honest we admit that our acquisition of the art is comparatively inadequate. To take a simple example. It is no great matter to be able to identify a cardiac lesion; the much more difficult art, as embodied in the anamnesis, is to consider how many of the symptoms presented are the result not of the structural lesion but of fear, anxiety, or uncertainty.

THE PATIENT'S COÖPERATION

When very young we arrogate our superiority; we disdain and execrate the layman's stupidity. With growing experience we develop more patience, we acquire an understanding and realise that it is we who are silly to expect too much from him. We come to excuse his inadequacy of expression, his over-anxiety to coöperate, his tendency to exaggerate in order to enlist our interest and attention, or, on occasion, his desire to minimise in an ostrich-like attempt to reassure himself that his condition is not serious. We learn to appreciate his point of view, why his ignorance of technicalities prevents him from distinguishing irrelevancies from essentials, when everything that he supposes to have a bearing on his problem is in his eyes of uniform value. Instead of protesting impatiently, we ought to smile indulgently at his emphasis on the exact weight of the crate of bananas that fell on his foot, and to realise that although to the surgeon the number of the motor-car that caused an accident is not of the slightest importance, it may be the only item of interest to the patient with an eye to compensation, or to the police with a prospect of legal proceedings.

I have had a frantic telephone message in the dead of night from an educated man unable to sleep through the pricking of conscience recalling that earlier in the day he had informed me that he was fifty-six, when in fact he would not reach this age until the end of the week. For all he knew, such a detail might be of profound significance in the understanding and correct treatment of his complaint.

The handicaps to which I have referred have to be accepted with appropriate adjustment. We must abjure excuses or refrain from describing as impossible what is more or less difficult. I recall an amusing complication when interrogating a sick Turk. I have not a single word of Turkish, but in the room I discovered a German with whom I could converse, albeit in halting fashion. He interpreted to another, who spoke German and Russian and in turn communicated to a third with knowledge of Russian and Turkish; and so by this polyglottic route the patient's symptomatology was eventually extracted.

A SENSE OF PROPORTION

Professor Platt has provided the text for my discourse and it is appropriate for me to refer further to his exposition. He tells us that in 82% of cases the diagnosis reached after history-taking was unchanged by subsequent examination or investigation. But he goes on to say that emphasis on the history takes into account much more than the patient's statements; how he walks, whether he is pale or flushed, thin or fat, exhibits tremors or facial paralysis, and the like. Now, with all respect, it seems to me that in his enthusiasm Professor Platt overstates his case. Such observations are not germane to his thesis; they are as much a part of physical examination as feeling the pulse or testing the reflexes.

Curiously enough it is the dermatologists who have been most vocal of all our colleagues in supporting Professor Platt. I say curiously enough, because one might have been tempted to conclude that, with essential lesions so accessible to direct observation, the patient's coöperation was relatively superfluous. But the dermatologist insists on the importance of finding out the exact site of the first appearance of a skin lesion and the exact moment of its onset. (I cannot help thinking that our colleague must have more intelligent patients than the general physician or is more skilful in dealing with them.) Further examples of the value of a history include the reminder that, if a housewife loses her rash while on holiday, we must expect something causal in her home environment, and that dermatitis may appear suddenly when a patient feels himself to be the victim of grave injustice, or be aggravated by delay in obtaining compensation.

In emulation of Professor Platt a dermatologist has published his own experience of deliberately averting his eyes from patients to test his ability to diagnose from description of the symptoms, even of the type of itching complained of.

We may admire the skill of an expert and accept as a tour-de-force such self-imposed limitations, but by these I am reminded of freak competitions, such as playing golf in boxing-gloves, or billiards with an umbrella stripped of a ferrule, or cricket left-handed with a broomstick. With these analogies before us we might issue an invitation or, shall I say, a challenge to examine a patient blindfold or with the ears tightly plugged with cotton-wool. There are occasions when interrogation is of supreme importance, but it is not

* Presidential address to the Section of Medicine, the Royal Society of Medicine, delivered on Oct. 26, 1948.

Digitized by Google

necessary for its appreciation to deprive oneself of all other assistance.

I advance this criticism in no spirit of depreciation but to preserve a sense of proportion in representing the proper rôle of the anamnesis.

UNNECESSARY INTERROGATION

There are occasions when unnecessary talking is worse than none; it wearies the interrogator and may alienate a patient, who, failing to see any connexion between the questions and his troubles, loses all interest as well as confidence in the doctor.

It is an absurd waste of time to cross-examine on the details of something which will be settled by brief inspection. I have felt strongly about this ever since as a house-surgeon I wasted a whole morning in a coroner's court impatiently enduring the catechism of eye-witnesses of a fatal street accident. The pompous old fool spent nearly three hours endeavouring to reconcile the contradictory statements relating to the side of the body on which the deceased had been struck by a motor vehicle. Finally I was called to describe the necropsy findings, and fifteen seconds sufficed to establish the truth beyond any doubt.

It is surely silly to expect any accurate information from descriptions requested of the appearance of the stools or other excretions. Even if the patient is inquisitive enough and has adequate opportunity for observation, his report cannot be regulated by scientific knowledge; he will give the answer apparently expected of him, and is more likely to be misleading than useful.

UNDERGRADUATE INSTRUCTION

Those of us who teach undergraduates enjoy a privilege which is a serious responsibility. Too uncompromising an insistence on an inflexible routine, a relic perhaps of our own student experience, may lead to boredom through its automaticity or to contempt because of its unreasonableness.

I quote from a work on clinical diagnosis:

> "Inquiry should be made as to whether any member of the family (parents, grandparents, brothers, sisters, uncles, aunts, cousins) have suffered from consumption, cancer, acute rheumatism, gout, nervous diseases, insanity, asthma, heart disease, apoplexy, and especially those diseases to which the patient himself seems liable."

In how many instances can such a detailed inquisition be profitably carried out? Most people have little enough reliable knowledge of their immediate relatives. To insist upon a stereotyped formula with the inclusion of a lot of irrelevant matter is to develop a Teuton type which is all right so long as the machine runs according to rules, but comes to grief through any deviation from orthodoxy. The intelligent student resents the implication that he is entirely devoid of independent thought and is not entitled to claim the ability to reason or use common sense. His note "family history nil ad rem" may be met with what seems to him an unreasonable rebuke that he is not in a position to judge whether anything is or is not pertinent, that he must record everything and leave deductions or conclusions to his seniors. Accordingly a contumacious rebel obeyed with the following strictly accurate but hardly relevant family history in the case of a sufferer from syringomyelia:

> "The patient's mother is living; she is 86 years of age and can walk to the nearest village, a distance of 2⅔ miles, in 1 hour 42 min. His father died at 88. I am unable to ascertain the cause of death, but from the description of immediately antecedent events it appears to have been from overeating. One brother was killed by falling (when sober) into a threshing-machine. Another ran away to sea at the age of 14 and has never been heard of since. He has one sister, and the only detail which the brother can supply is that she has had 19 children."

It seems to me that, provided reasonable explanations are forthcoming, any clinical clerk will be prepared to coöperate, appreciating that he is a cog in a mighty machine, and that upon individual apparently trivial items statistics are founded and constitute the vast subject of familial incidence and proclivities. This, we must explain, is his personal contribution quite apart from his education, and interest will not be prejudiced when inexorable orthodoxy is not enforced but the significance of details is explained and appropriate concessions are permitted. In this way he may regard himself as already a member of a cultured profession and not a mere copying clerk.

THE PERSONAL HISTORY

I feel that I need no further protestations of a tepid regard for family history. The patient's previous illnesses deserve far more attention for their influence on subsequent occurrences may be considerable. The scope of personal history, being individual, is almost unlimited. Up to a point this must be a stereotyped routine, but on the social and psychological side it is, as I have presumed to say, almost unlimited. It is not enough to decide that a patient's indigestion is of a so-called functional character, by which we mean that her nerves are responsible for aberrations of motility and secretion in perfectly sound organs so that ordinary occurrences normally unperceived find their way into consciousness with inevitable misinterpretation. Prescription of a sedative is a poor substitute for the enterprise of discovering what adverse influence is responsible and what must be attempted in the way of removal. Such indigestion may be the result of food allergy, of constipation, of faulty or unhygienic habits, or of domestic infelicity; and history-taking in such circumstances demands the finesse of a diplomat with the sympathy of a father-confessor in the understanding that the sorrow that has no vent in tears makes other organs weep. We can hardly teach our students any general rules of procedure. They should learn by watching us who may claim to be experienced. What to the neophyte may seem a smart piece of detective work is to the senior only the obvious.

Some years before the late war I was asked to see a case of unexplained pyrexia when everything had been thought of with appropriate investigations—everything, that is, but one thing. Maybe I hit upon the diagnosis by studying the temperature chart, but I like to believe it was because I had pursued the history and learnt that the man had been on a tramp steamer which a month back had touched at a West African port—hence malaria.

Admittedly there is the danger of obsession and of forcing our own thoughts into the patient's mind to discover what one expects to find. The psychosomatic association is the correct approach. But how easy it is to come down heavily on one or the other side. Consider a psychologist's interpretation of what are generally regarded as commonplace physical disturbances. To him, cardiospasm symbolises an insult the patient cannot swallow; vomiting, an aversion to some task or situation of which he is literally as well as metaphorically sick; lumbago, a reluctance to stoop and lower himself to a certain course of action; prolonged weakness attributable to post-influenzal toxæmia, the reaction of the patient's knowledge that her mother-in-law is coming for a long visit as soon as she is well enough to entertain her.

THE ANAMNESIS IN ABDOMINAL DISEASE

Moynihan said of duodenal ulceration "the history is everything, the physical examination nothing"; an exaggeration, of course, but doubtless deliberate to indicate the relative importance. In most instances we expect to find but little in the clinical examination of the abdomen, whether a functional disturbance or a structural lesion is responsible for the symptom.

Digitized by Google

With adequate patience and the resolution to avoid prepossessions and precocious conclusions, an accurate diagnosis will be determined in most gastro-intestinal complaints; and if subsequently we are compelled to acknowledge a mistake we can generally discover the cause by retracing our steps in the performance of the anamnesis. Since subjective phenomena cannot be measured, weighed, or photographed, mistakes must inevitably be in proportion to the physician's inability to assess descriptions at their proper value.

THE PROBLEM OF PAIN

Although it is particularly of gastro-intestinal diseases and disorders that one is thinking, it is convenient to consider pain in general, and I cannot do better than refer to the criteria elaborated by Professor Ryle:

(1) What is the *character* of the pain? Admittedly, too much reliance must not be placed upon a patient's terminology. But valuable information is sometimes obtainable from such descriptions as "gnawing" in the case of peptic ulcer, "bursting" in the case of gall-stones, "colicky" in enteritis, "vice-like" in angina, or "burning," which is almost invariably functional and not structural in origin, and curiously frequent among Hebrews.

(2) *Severity* introduces the same difficulty. The "discomfort" advanced by one sufferer is regarded by another as "agony," and we have no means of standardising the level of the threshold of any sensation; but at least some idea may be gained by the demand for morphine to relieve or by a history of interference with sleep.

(3) The *situation* is sometimes a guide to causation when anatomical relationship is considered, especially as regards referred pain.

(4) The *duration* and the *continuity*. In these connexions the difference between angina pectoris and coronary occlusion is recalled.

(5) The *time* of occurrence, particularly with a constant relation to meals or effort. The irregular appearance of attacks of pain quite out of the blue suggests tabes.

(6) The method of *relief*—e.g., by alkalis, food ingestion, amyl nitrite, or abdominal pressure. The pain from a diaphragmatic hernia is relieved by moving about, in striking contrast to angina, which it may closely resemble.

(7) The influence of any factor that *aggravates*—e.g., exertion, jolting movements, cold, emotion, fatigue, worry, and tobacco.

To apply these criteria, by way of example, Professor Ryle analyses the features of spasm of the colon, which has to be differentiated from appendicitis, duodenal ulcer, diverticulitis, carcinoma of the colon, renal and biliary colic, and ovarian or tubal disease. Thus:

The character of the pain: dull, steady but bearable.

Its situation: along the course of the colon.

Its duration: protracted and continuous.

Its frequency: variable.

It depends on environmental factors: aggravated by cold, fatigue, worry, tobacco, and purges; relieved by warmth, belladonna, freedom from mental disturbances, and holidays.

Such care in the analysis of an anamnesis pays dividends. A diagnosis will be confidently established, possibly in opposition to radiological evidence or other accessory aids by which a pusillanimous clinician may be unduly influenced.

To adopt the phraseology of a sister profession, medical history may be regarded as circumstantial evidence. To continue the parallel we are rarely provided with obvious clues, still more seldom with the opportunity to convict *in flagrante delicto*.

In this respect the examining physician has to be judge, jury, and prosecuting and defending counsel all in one. A reminder is perhaps pertinent that circumstantial evidence, however approbated, may well be fallacious. Mark Twain's humorous example may be recalled. Eye-witnesses will unanimously testify to the employment of a penknife by a woman who has sharpened a lead pencil, when inspection would be overwhelmingly in favour of her having used her teeth.

A pessimistic critic has described the case-history as a coagulated jumble of fact, speculation, suggestion, rumour, invention, inaccurate statements, imperfect reminiscences, vague opinions, and reports. Well, perhaps the truth is approached because many of these errors cancel each other, especially when in interrogation common sense is used with common sense, and a place is retained for insight and sympathy.

RETINAL AND VASCULAR DAMAGE IN LONG-STANDING DIABETES

J. HALLIDAY CROOM
B.A. Camb., M.B. Edin., F.R.C.P.E.
ASSISTANT PHYSICIAN

G. I. SCOTT
M.A., M.B. Edin., F.R.C.S.E.
ASSISTANT OPHTHALMIC SURGEON

ROYAL INFIRMARY, EDINBURGH

IT is well known, and has been shown by both Joslin (1946) and Stocks (1944), that diabetics are living longer, and that the cause of death in diabetes has changed materially since the introduction of insulin. It therefore seems reasonable to assume that the number of diabetics showing degenerative lesions is increasing. The view that degenerative changes are inevitable, provided that the diabetic lives long enough, has been put forward by Dolger (1946, 1947), Mirsky (1945), Rosenbusch (1945), and Priscilla White (1941), and emphasised in the *Journal of the American Medical Association* (1947).

Kimmelstiel and Wilson (1936) described a syndrome of intercapillary glomerulosclerosis occurring in diabetes, usually long-standing, with hypertension, œdema of the nephrotic type, massive albuminuria, and renal or cardiac decompensation. They pointed out, however, that only a small proportion of cases of diabetes appear to show this lesion at necropsy. Since then several workers have claimed that this condition is not uncommon. Siegal and Allen (1941) found it at necropsy in 35 of 105 diabetics without hypertension or signs of renal deficiency, and in 14 of 18 diabetics with clinical evidence of renal damage. Laipply et al. (1944) found it common in diabetics at necropsy and considered it more specific, as an indication of diabetes, than hyalinisation of the islets. In their experience, however, the nephrotic syndrome was not a common clinical feature, since it occurred in only 6·3% of their diabetic patients showing intercapillary glomerulosclerosis post mortem. They also found no relation between the degree of its development and the duration or severity of the diabetes.

Dolger (1946, 1947), from careful study of 200 patients who developed diabetes before the age of fifty, concludes that the duration of the diabetes is the most important factor in the development of degenerative changes. He found that, in patients with diabetes of twenty-five years' duration, not 1 in 200 escaped retinal hæmorrhage, regardless of age of onset, severity of diabetes, or type of treatment used. He is of the opinion that retinopathy usually precedes other signs of vascular degeneration, though half his patients exhibited hypertension and albuminuria at the time of earliest retinal hæmorrhage. Dolger therefore believes that present-day treatment of diabetes has not averted the vascular complications which he considers an associated phenomenon rather than a complication. He also thinks that progressive vascular damage, such as intercapillary glomerulosclerosis, originally described by Kimmelstiel and Wilson (1936), exists with various degrees of severity in every case of diabetes mellitus of long standing.

Graham and Oakley (1938), on the other hand, from analysis of 100 diabetic patients attending a follow-up

Digitized by Google

department, concluded that neither the duration of the diabetes nor its severity played any part in causing ocular complications, which they noted in 32% of their patients. As regards cardiovascular complications, however, they found that, though the severity of the diabetes did not appear to play any part in these changes, they occurred more often in patients in whom the disease was of long standing. They also thought that diabetes had no special effect in raising the blood-pressure.

Lichtenstein (1945) describes his findings in 169 cases of diabetic children and young persons up to the age of twenty-nine observed over ten years. His patients were treated with insulin but without dietetic restriction; yet he noted no rise in blood-pressure and no X-ray evidence of calcification of blood-vessels—a finding in contrast to that of Priscilla White (1941), who found that, of 150 cases of about the same type observed for over fifteen years, 1 in 6 had arteriosclerosis in the second decade, and 1 in 5 in the third decade.

RETINOPATHY

Though specific changes in the fundi of diabetics were first described by Jaeger in 1856, and elaborated by Hirschberg in 1890, there is still controversy over their nature and incidence. Some workers hold that, while certain features enable such changes to be distinguished from retinopathy of other types, the condition is essentially a modified form of arteriosclerotic retinopathy. Others maintain that there is a form of retinopathy peculiar to diabetics, which can develop in the absence of raised blood-pressure, impaired renal function, or clinical evidence of arteriosclerosis.

Foster Moore (1920), while emphasising the characteristic features of diabetic retinopathy, found that patients showing retinal changes usually had arteriosclerosis too. Gray (1933), however, in a review of 66 cases of diabetic retinopathy, found that sclerotic changes in the retinal vessels were slight or absent, but that more than half his patients had a raised blood-pressure. He therefore considered hyperpiesis at least a factor in the production of the retinopathy.

Ballantyne (1945), discussing the retinal changes associated with diabetes and hypertension, has expressed the opinion that diabetic and hypertensive retinopathy must be regarded as two separate entities, and in a large series of diabetic patients Ballantyne and Loewenstein (1943) found that half of those with retinal changes had normal blood-pressure, and that many showed no arteriosclerotic changes in the vessels.

It is also significant that, though Wagener and Wilder (1921) thought that the retinopathy of diabetics was essentially that of arteriosclerosis, Wagener (1945), as a result of twenty-five years' further clinical experience, came to believe that neither arteriosclerosis nor hypertension produces retinopathy of the type characteristic of diabetes.

The next most notable feature about diabetic retinopathy is the diversity in the published figures of its incidence, varying from 5·2% (Joslin 1928) to 29·6% (Wagener 1945). As Duke-Elder (1940) has pointed out, this variation may be partly due to the inclusion of children in some statistics, and partly to the degree of vascular change recognised as pathological by different observers. A further difference will arise, however, depending on whether cases are selected from those attending diabetic clinics or ophthalmic departments, since many patients may make no complaint about their eyes and therefore may not come under the observation of the ophthalmologist.

Wagener (1945) reviews the opthalmoscopic findings in 1021 diabetics examined at the Mayo Clinic in 1944. Retinopathy of the type characteristic of diabetes was present in 29·6%. In comparing these figures with observations published by Wagener and Wilder (1921) and Wagener et al. (1934), Wagener (1945) emphasises that the incidence of retinopathy had increased from 8·3% in 1921 to 17·7% in 1934, and 29·6% in 1945. When the incidence was correlated with the duration of diabetes, however, it was found to be only 10·7% in those who were known to have had diabetes from eleven to fifteen years, but to be 73% in those who had had diabetes longer than twenty years.

PRESENT INVESTIGATION

We have examined 60 patients with diabetes, who have had the disease from fifteen to twenty-six years, the average duration being 18·7 years. Of the 60 patients 28 were males and 32 females. The age-distribution is shown in fig. 1.

Clinical Examination

Of the 60 patients examined, 15 were free from evidence of degenerative disease—i.e., their hearts were not enlarged, their blood-pressures were below 140/90 mm. Hg, their peripheral vessels were not thickened, their dorsalis-pedis pulses were easily palpable, and they had no evidence of diabetic retinopathy or of arteriosclerotic change in their retinal vessels. The duration of the diabetes in these 15 cases was as follows: fifteen years 1 case, sixteen years 3 cases, seventeen years 3 cases, eighteen years 2 cases, twenty years 3 cases, twenty-one years 2 cases, and twenty-six years 1 case. The age of onset of diabetes in these cases varied from three to forty years, the ages at the time of observation varying from twenty-one to sixty years.

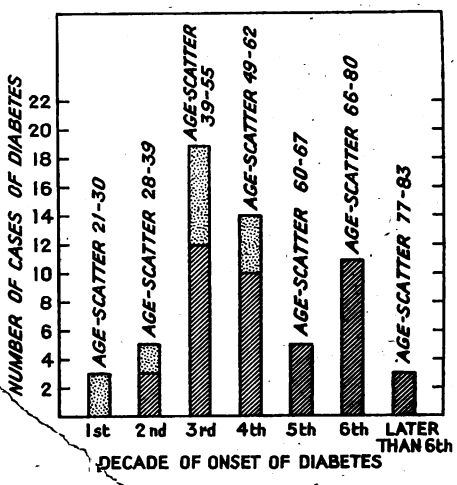


Fig. 1—Age-distribution of 60 diabetics, showing presence (hatched columns) or absence (stippled columns) of vascular complications in relation to decade of onset of diabetes.

In this series it therefore seems that such degenerative lesions are not inevitable, even as late as twenty-six years from the onset of the diabetes.

Albuminuria and œdema were present in 2 cases only, suggesting that the nephrotic syndrome associated with diabetes is a clinical rarity, as suggested by Kimmelstiel and Wilson (1936).

In 23 cases the systolic pressure was below 140 and the diastolic pressure below 90; these were classified as normal. In 26 cases the systolic pressure exceeded 160 or the diastolic exceeded 100; these were classified as hypertensive. The remaining 11 cases were classified as doubtful, the systolic pressure being between 140 and 160, and the diastolic between 90 and 100. The distribution of these cases is shown in fig. 2. It will be noted that a considerable number of cases with retinopathy had no evidence of hypertension.

Of the patients classified as hypertensive 3 only were below the age of fifty, whereas 5 patients with normal blood-pressure were aged fifty-one, fifty-six, fifty-nine, sixty, and seventy-six.

The heart was clinically enlarged in 11 patients, all of whom had hypertension. In this group 1 patient had angina of effort, 1 had frequent extrasystoles, and 1 had aortic stenosis. In addition, 1 of the younger patients had rheumatic mitral disease without cardiac enlargement.

The peripheral vessels were definitely thickened in 15 patients of whom 13 were aged over sixty. The dorsalis-

Digitized by Google

pedis pulses could not be felt in 4 cases, and were felt with difficulty in a further 3.

A careful analysis of the case-records was made in an attempt to assess the relation between the severity or control of the diabetic state and the development of complications. The notes date from the patients' first attendance fifteen to twenty-six years ago and provide a continuous record of their condition on each visit to the dietetic outpatient department. The severity of the diabetes was assessed by the dosage of insulin required and the control of the condition by the general well-being of the patient, the degree of glycosuria, and the frequency of reactions. In this series there was no significant correlation between the severity of the diabetes or the control of the diabetic state and the development of cardiovascular complications.

Ophthalmological Findings

The fundi were examined in detail after dilatation of the pupils with a mydriatic. Particular attention was paid to the state of the retinal vessels and to the presence or absence of hæmorrhages or exudates. A search was also made for the capillary micro-aneurysms described by Ballantyne and Loewenstein (1943). The presence of micro-aneurysms, hæmorrhages, or exudates, was taken to signify retinopathy. As criteria for recording the presence of arteriosclerosis in the retinal vessels we used any or all of the following signs:

(1) Constriction at the arteriovenous crossings.

(2) Visible changes in the walls of the arteries.

(3) Irregularity in calibre of the arteries.

(4) Narrowing of the arteries, if sufficiently well marked to be undoubtedly pathological.

Tortuosity of the vessels, changes in the reflexes, and slight degrees of narrowing were not, in themselves, regarded as definite signs of pathological change. The ocular findings were recorded independently of the general medical examination, the results being correlated at the end of the investigation.

Changes typical of diabetic retinopathy were present in 18 patients—nearly a third of the group examined. Characteristic hæmorrhages or exudates were found in 16. Micro-aneurysms were seen in 5 patients, and were the only sign of retinopathy in 2 of these cases. The hæmorrhages were mainly deeply situated, small, and sharply circumscribed though a few were superficial and "fleaky," 2 cases showed larger "hæmorrhages which appeared almost subhyaloid. The exudates were of the usual type, being white and well defined and tending to be aggregated nearer to the macula than were the hæmorrhages, which varied in their distribution, but the macula itself was only involved in 3 cases. Micro-aneurysms were most numerous temporal to the optic disc, but isolated aneurysms were also seen in the nasal half of the retina and could be distinguished from the minute hæmorrhages by their clear definition and the fact that they were venous in colour.

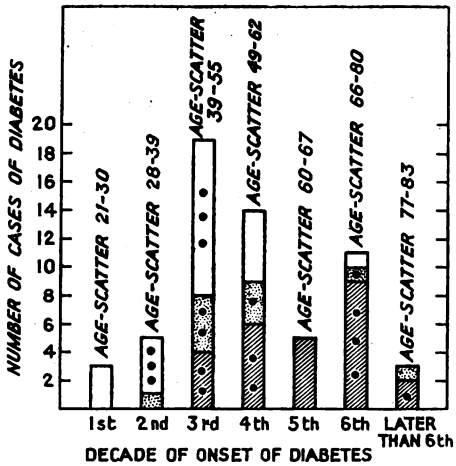


Fig. 2—Relationship of retinopathy to state of blood-pressure in 60 diabetics: blank columns, normal blood-pressure; stippled columns, abnormality of blood-pressure doubtful; hatched columns, raised blood-pressure. Each dot signifies one case of retinopathy.

In 2 patients with retinopathy, severe hæmorrhages into the vitreous and subsequent retinitis proliferans developed.

Engorgement of the retinal veins, though evident in most of the cases of retinopathy, was not pronounced; and, if attention had not been drawn to pathological changes such as micro-aneurysms, hæmorrhages, or exudates, the congestion of the veins in many cases might well have been classified as within physiological limits.

Arteriosclerotic changes in the vessels were minimal or absent, and 9 of the 18 patients with retinopathy showed normal retinal arteries. It must be emphasised that the arteriosclerotic changes, when present, were all slight. They were limited to a slight constriction at the arteriovenous crossings, except for 1 patient with well-marked hypertension who exhibited a "mixed" arterio-sclerotic and diabetic retinopathy, and 1 or 2 other hypertensive patients who showed pathological narrowing of the arterioles. The incidence of retinal "arterio-sclerosis" in patients with and without retinopathy is compared as follows:

Retinal vessels	*With retinopathy*	*Without retinopathy*
"Normal"	9	28
Slight arteriosclerosis but associated with hypertension	4	12
Slight arteriosclerosis unassociated with hypertension	5	2
Total	18	42

It will be seen that "arteriosclerotic" changes in the retinal vessels are more common in cases with retinopathy than in those without. The fact, however, that the retinal vessels were normal in half the cases with retinopathy suggests that some factor other than arteriosclerotic change is concerned in its production.

That diabetic retinopathy can develop in the absence of hypertension has already been shown (fig. 2). In addition it should be noted that two-thirds of our cases with retinopathy had no clinical evidence of general arteriosclerosis.

It seems, as Ballantyne and Loewenstein (1943) have suggested, that the capillary micro-aneurysms occurring with normal or practically normal retinal vessels are probably the earliest diagnostic sign of diabetes, so far as ocular findings are concerned.

The absence of retinal arteriosclerosis in cases with retinopathy is in contrast to the observations recorded in many textbooks. This apparent contradiction is probably explained by the fact that many of the published reports deal with cases seen in ophthalmic departments, where the patients most commonly seen are elderly diabetics who show a mixture of arteriosclerotic and diabetic retinopathy. Many of our patients, as already noted, did not complain about their vision, since the hæmorrhages or exudates involved the macular area in only a few cases, and they would therefore not normally come under the observation of the ophthalmic surgeon.

SUMMARY

A series of 60 patients who have had diabetes from fifteen to twenty-six years have been examined clinically and ophthalmologically.

Vascular and retinal complications are not inevitable, even as late as twenty-six years after the onset of diabetes.

Clinical evidence of diabetic intercapillary glomerulosclerosis, as shown by the development of a nephrotic syndrome, was found in only 2 cases.

Diabetic retinopathy was observed in some cases without signs of hypertension or of generalised arteriosclerosis.

Digitized by Google

Arteriosclerotic changes in the retinal vessels were either absent or minimal in most of the cases with retinopathy, and 9 of the 18 patients with retinopathy had normal retinal arteries. It therefore seems that some factor other than arteriosclerotic change must be mainly responsible for the production of retinopathy in diabetes.

There did not appear to be any correlation between the vascular or retinal changes and the severity or control of the diabetic state.

We are indebted to Prof. D. M. Dunlop, at whose suggestion the investigation was made, for much helpful advice and criticism in the preparation of this paper, and for permission to use the facilities of his department. We also wish to thank Miss A. Buchan, superintendent dietitian, for her assistance.

REFERENCES

Ballantyne, A. J. (1945) *Arch. Ophthal., N.Y.* **33**, 97.
— Loewenstein, A. (1943) *Trans. ophthal. Soc. U.K.* **63**, 95.
Dolger, J. (1946) *Bull. N.Y. Acad. Med.* **22**, 482.
— (1947) *J. Amer. med. Ass.* **134**, 1289.
Duke-Elder, W. S. (1940) Text-Book of Ophthalmology. London; vol. III.
Graham, G., Oakley, W. G. (1938) *St. Bart's Hosp. Rep.* **71**, 43.
Gray, W. A. (1933) *Brit. J. Ophthal.* **17**, 557.
Hirschberg, J. (1890) *Dtsch. med. Wschr.* **16**, 1181, 1236.
Jaeger, E. (1856) Beiträge zur Pathologie des Auges. Vienna; p. 33.
Joslin, E. P. (1928) The Treatment of Diabetes Mellitus. 4th ed., Philadelphia.
— (1946) *Ibid.* 8th ed., Philadelphia.
Journal of the American Medical Association (1947) **134**, 608; **135**, 1074.
Kimmelstiel, P., Wilson, C. (1936) *Amer. J. Path.* **12**, 83.
Laipply, T. C., Eitzen, O., Dutra, F. R. (1944) *Arch. intern. Med.* **74**, 354.
Lichtenstein, A. (1945) *Acta pediat.* **32**, 556.
Mirsky, I. A. (1945) *Proc. Amer. Diabetes Ass.* **5**, 117.
Moore, R. F. (1920) *Trans. Ophthal. Soc. U.K.* **40**, 15.
Rosenbusch, H. (1945) Prognose und Spätkomplikationen des Diabetes Mellitus in Kindesalter. Basle; p. 78.
Siegal, S., Allen, A. C. (1941) *Amer. J. med. Sci.* **201**, 516.
Stocks, P. (1944) *J. Hyg., Camb.* **43**, 242.
Wagener, H. P. (1945) *Proc. Amer. Diabetes Ass.* **5**, 203.
— Dry, T. J., Wilder, R. M. (1934) *New Engl. J. Med.* **211**, 1131.
— Wilder, R. M. (1921) *J. Amer. med. Ass.* **76**, 515.
White, P. (1941) *New Engl. J. Med.* **224**, 586.

DEATHS FROM VAGAL INHIBITION *

KEITH SIMPSON
M.D. Lond.
READER IN FORENSIC MEDICINE IN THE UNIVERSITY OF LONDON, AT GUY'S HOSPITAL

THE investigation of sudden deaths from obscure or uncertain causes is one of the more responsible duties of the coroner or procurator-fiscal, and he has come to rely on necropsy to elucidate such deaths. As the statutory use of "any registered medical practitioner" for such onerous and meticulous technical tasks has gradually given way to the employment of properly trained pathologists, so has the standard of observation and inference improved.

Many previously unrecognised causes of death have come to light as a result of these improved standards of technique: air and fat embolism, allergic and anaphylactic phenomena, transfusion accidents and incompatibilities, spasmodic hypoglycæmia, adrenal exhaustion, and other fatal events with a scanty morbid anatomy are all examples of increased exactitude in the assessment of death. Bad necropsy technique or sheer ignorance can alone overlook such conditions.

But the precise nature of all sudden deaths is not revealed by organic changes of this kind: despite the most meticulous examination, nothing is found in some cases.

Finding nothing has, in the past, been too much of a responsibility for many pathologists, and the belief grew that perhaps there were certain types in whom sudden death was an ever-present sword of Damocles likely to drop without warning. To be able to point to *anything* would afford *some* satisfaction, and the thymus gland and lymphatic tissues, which are commonly strikingly prominent in children and adolescents, offered a solution. "Status thymolymphaticus" grew to provide the perfect answer to a death the cause of which had not been identified. This myth, like all myths, had just enough factual basis to justify the interest taken in it; the thymus *was* remarkably prominent in many sudden deaths—an abnormality of some frequence but by no means a constant abnormality.

The Pathological Society made a careful pathological study of 600 cases of sudden death in apparently healthy young people under the age of 15, and Young and Turnbull (1931) published their famous report to the effect that, though considerable variations in the size of the thymus existed, they found no evidence that so-called status lymphaticus had any existence as a pathological entity. THE LANCET (1931) issued an obituary notice in the form of a leading article, and later Cohen (1936) agreed that the term as used in the coroners' courts in relation to the cause of death was "a meaningless expression." But convenient traditions die hard, and Taylor in 1939 again raised this old bogy at the Royal Society of Medicine in reporting 14 deaths in which, after necropsy, he felt the only explanation was an excess of lymphoid tissue. Further, Millar and Ross (1942) introduced a new aspect of the theory by reporting aortic and other vascular hypoplasia in association with prominent lymphoid tissues as an explanation of sudden accident or of accident-proneness. Once again THE LANCET (1942) replied squarely to this attempt to revive the tradition by an annotation entitled The Nine Lives of Status Lymphaticus, and nothing has been heard of the matter since—except in one far more reasonable respect.

In adrenal insufficiency states, both naturally in man (Addison's disease) and experimentally in animals, it had often (Star 1895, Wiesel 1904, Hedinger 1907) been remarked that there was an unusually predominant lymphoid tissue. "Status lymphaticus" was attributed to hypoplasia of the chromaffin system, and attention was drawn to the heightened susceptibility to injury, infections, indeed any noxious agent. Was it possible that the status was in fact a state of adrenal insufficiency? The evidence is not yet clear, but one aspect of it is. A precipitatory factor has still to be identified, even if this status is assumed to be established (Campbell 1937); some last straw operates to precipitate death. It is not enough to point to a "status" like adrenal hypoplasia or lymphoid hyperplasia and to say there is the cause of instant death in a fit person—any more than dwarfism, flat-feet, or obesity.

Examination of the events leading up to the time of death and the form of dying may make it clear that no time sufficient for the development of any material organic change—even a biochemical reverse like anoxia or alkalosis—can have elapsed. Some functional lapse alone could afford an explanation; the most acceptable being, naturally, some cause for sudden complete inhibition of the heart's action, for this alone causes literally instant death.

Where a healthy, if somewhat nervous, young girl aged 22, plainly very fit and well, anticipating with great pleasure the completion of a normal 3 months' pregnancy, walks to a kitchen tap, fills a glass with cold water, is seen to drink it off and collapse instantly to the floor dead, some sudden inhibition of function is almost certain. Necropsy in this case revealed nothing to explain the circumstances—literally no change whatsoever.

It is to an analysis of some 87 such deaths that I apply, as must be, basic principles. It is not a matter of evaluating morbid anatomical or histological findings, but of reasoning the possibilities of some physiological upset which could account for death.

PHYSIOLOGICAL CONCEPTS

The mechanism of the regulation of circulatory volume and pressure has been securely established since Bayliss

* Lecture given at the Royal College of Surgeons on Nov. 18, 1948.

Digitized by Google

(1923) first envisaged a vasovagal tonal control. Further work by Heymans and Bouckaert (1939) demonstrated the sentinel-like aortic bodies and the carotid body spread over the arch of the aorta and the carotid artery bifurcation respectively. The balance of both depressor and pressor influence demands that both vagus and sympathetic nerves shall be intact. Over-use of the vagal trunk leads to slowing of the heart, contraction of the coronary vessels, and dilatation of the splanchnic vessels. A positive depression of the heart-rate ensues, the rhythm slowing or being interrupted, sometimes permanently with the result that death follows instantly.

The stimuli which excite such responses may develop naturally from the aortic or carotid bodies. Any rise in arterial pressure sets this reflex in motion, bringing quick relief through the afferent depressor fibres of the vagus. In addition—and here I come to the basis of the functional catastrophe of vagal inhibitory death—afferent stimulation of this reflex may come from many other sources. The sensory nerves of the skin, of the pharynx and glottis, of the pleura, of the peritoneum covering the viscera and extending into the spermatic cord, of the cervix, of the urethra, and of the perineum carry afferent fibres of what used to be called protopathic type which pass into the lateral tracts of the spinal cord and thence to the brain, and also effect local reflex connexions at the same level. The spinal tracts effect synaptic connexion with the vagal nucleus and may thus initiate a slightly more lengthy reflex arc. This may clearly be facilitated from both the sensory central cortex and from the thalamic centres. It is these which may reflect emotional influences in the effectiveness or otherwise of the reflex.

The vagal nerve centre may be stimulated instantly by this mechanism and respond through its efferent fibre by depressor action in no more time than is required for any such reflex. This interval of time is far too short for the development of material changes in oxygen or pH, to either of which the vagal centre, like other vital medullary centres, is particularly sensitive. Similarly, a falling blood-pressure, the production of toxic metabolites, adrenin, and sympathin all require time for their effective development—too long to justify their consideration in explaining so instant a phenomenon. It is clear that the catastrophic suddenness of vagal inhibition can only be explained as a neural reflex conditioned by some sharp stimulus.

For example, a grandfather of 71, first to be served at a Christmas party, fell to with precipitate eagerness, thrusting a substantial piece of steak into his mouth. He was seen to stop dead in the act of raising his fork and to fall back motionless, dead. Necropsy revealed a large mass of meat lodged across the glottis, but no asphyxial changes whatsoever.

In another case a soldier on leave was dancing with a girl, when he edged her to a corner and, placing his hand across the front of her neck, he "tweaked it playfully"—a mere momentary tightening. She immediately collapsed to the floor, lay still, and did not draw another breath: she was dead.

This instant failure can only be functional—a nervous reflex inhibition—and, since the depressor action of the vagus is well recognised, can be reproduced by similar conditions experimentally, and operates with the same lightning effect, it is reasonable to assume that this is the mechanism of such deaths.

The heightened response, whether it be a facilitation mechanism or not, plainly lies partly under the control of the sensory motor cortex and of the thalamus, the latter possibly initiating emotional conditioning.

Lewis (1932) has emphasised the variable vagal tone shown by different people and even by the same people at different times, which results from this facilitation. The initial strength of the afferent sensory stimulus probably does not matter greatly, though the "all or nothing" principle does not apply as a simple "law." The effect on the synapse of conditioning by temperament, emotion, nervousness, or apprehension is considerable. It is common knowledge in practice that a fatal vagal inhibition is likely only if the emotional tension is high.

A well-known example of this is that of the Scottish janitor who had achieved a considerable unpopularity with his students and was the victim of a mock execution staged with impressive ceremony. He was led to the guillotine, jeered and cursed, blindfolded, and forced down on to the block. He was in terror as last rites were read, and collapsed and died the instant a wet towel was flicked in mock execution across the back of the neck.

In a case coming through my own hands, a nervous young man told his father "If they needle me again I'll die"—and he did. He was in a taut apprehensive state when the doctor came to the bedside to remove chest fluid which had again accumulated, and he died instantly the moment the needle reached the pleura. Necropsy revealed no organic cause.

Anæsthesia reduces the risk of such violent depressor discharges, perhaps by removing the elements of sensation and the emotional facilitation. Any anæsthetist of experience has noted the momentary disturbances of rhythm in both respiration and pulse that accompany certain surgical procedures, such as herniotomy, dilatation of urethral or anal sphincter, sudden traction on dilatation or emptying of a vessel, usually at the end of operation or when anæsthesia is being maintained at a very light level.

I examined a case during the blitz period in which temporary disturbance of the rhythm of breathing developed twice during a thyroidectomy, each time as the vagus sheath was displaced by forceps. Finally the surgeon lifted the sheath by forceps for final inspection, only to have the patient immediately cease breathing. The pulse and heart beat could not be felt, and no recovery followed.

The damping effect of anæsthesia can be the only explanation of the gynæcological surgeons' freedom from the danger—well known to every habitual criminal abortionist—of sudden fatal reflex collapse during the passage of instruments into the canal of the cervix, or even from sudden hot or cold douching in tense subjects.

INCIDENCE OF FATAL REFLEXES

In a series of fatal cases the following sources of reflex inhibition were established:

Obstetric (19):		*Bladder and Urethra* (13):	
Instrumental	9	Passing instrument	7
Abortion (with instrument)	4	Circumcision	3
Inversion	2	Repair of bladder	1
Antepartum hæmorrhage	1	Fitting urethral cast	1
Placental extrusion	1	Impacted calculus	1
Dilatation and curettage	1	*Carotid Sheath* (9):	
Rupture of uterus	1	Manual strangulation	6
Serous Membrane (18):		Thyroid operation	2
Peritoneal operation (hernia 6, general 3, pelvic 2)	11	Branchial cyst	1
Perforated ulcer	3	*Source of Vagal Reflex in fatal cases*:	87
Joint and bursa	2	Obstetric	19
Pleura	2	Serous membrane	18
Throat and Glottis (17):		Throat and glottis	17
Foreign body	7	Bladder and urethra	13
Water (immersion 3, drinking 1)	4	Carotid sheath	9
Intubation	4	Skin	4
Anæsthetic gas	2	Cardiovascular	3
		Alimentary (viscus)	3
		Peripheral nerve	1
		Total	87

I have already referred to the dangers inherent from this reflex during ordinary operative, obstetric, and anæsthetic procedures, even when carried out with reasonable care. Every surgeon and anæsthetist of experience has had the mortification of having a patient on whom skill and care have been expended die suddenly from fatal inhibition due to some trivial event. The important influence of adequate narcosis or anæsthetisation in minimising the violence of the reflex cannot be overemphasised. It is common, in my experience, to have both experts realise, when it is too late, that prolongation of anæsthesia while the peritoneal layer or deep sutures were being finally secured might have averted the issue, or to appreciate that in the apprehen-

Digitized by Google

sive patient paracentesis, injection of piles, and urethral instrumentation—or even mere removal of a dressing from a painful wound—are more safely accomplished under narcosis.

It is not, I am sure, generally appreciated how trifling the action which initiates reflex inhibition may be—how reasonable and proper in better circumstances.

FORENSIC ASPECTS

The forensic aspects of vagal inhibition deserve special attention in several respects. Its association with entirely unexpected sudden death has two most important aspects:

(1) Mentally defective persons and those of unsound mind—less commonly those who from gluttony or mere eagerness bolt their food—may die instantly from impaction of food in the glottis. There is no time for treatment of any kind, even if the cause of sudden death is appreciated; and no criticism of nursing or other hospital staff, in whose care such persons may be at the time, should follow. The use of terms like "choking" and "asphyxiation" can only be regarded as unhappy in these circumstances and likely to reflect on the staff without good reason.

2. Victims of some unlawful act, such as rape, may die suddenly in consequence of the pinning grip set by the hand across the throat—a common enough event in passionate intercourse. The subject of such a grip may suddenly die from vagal inhibition, no element of asphyxia having entered into the causation of death, and no intention of killing having ever entered the mind behind the gripping hand. If death ensues during the course of a felonious act, such as rape, the charge is one of murder, and it may reasonably be felt that such a charge in such circumstances is harsh. When vagal deaths ensue on criminal instrumental abortion, the charge is reduced to manslaughter or even the unlawful use of an instrument. Doctors acquainted with the possibilities of reflex vagal inhibition may feel that it is in the best interests of fair and real justice that the courts shall be left in no doubt how unexpected and unintentional death may have been.

REFERENCES

Bayliss, W. M. (1923) The Vaso-Motor System. London.
Campbell, E. H. (1937) *Penn. med. J.* **41**, 407.
Cohen, H. (1936) *Practitioner*, **136**, 252.
Hedinger, E. (1907) *Frankfurt. Z. Path.* **1**, 527.
Heymans, C., Bouckaert, J. J. (1939) *Ergebn. Physiol.* **41**, 28.
Lancet (1931) i, 593.
— (1942) ii, 732.
Lewis, T. (1932) *Brit. med. J.* i, 873.
Millar, W. G., Ross, T. F. (1942) *J. Path. Bact.* **54**, 455.
Star, P. (1895) *Lancet*, i, 284.
Taylor, J. R. (1939) *Proc. R. Soc. Med.* **33**, 119.
Wiesel, J. (1904) *Virchows Arch.* **176**, 103.
Young, M., Turnbull, H. M. (1931) *J. Path. Bact.* **34**, 213.

"... Formerly, a scientist thought out or encountered a problem and started working on it. As often as not he found something in the course of the work which led him in a new direction. An occasional observation, which most others would have overlooked, led the born researcher into new fields, an unexpected flash of an idea opened new vistas and led to solutions or to more problems. All great ideas and all great discoveries in the realm of pure science have come into existence this way. But now a man does not work on some subject or problem. He has a 'project.' A plan has been laid out, even worked out in all detail, a staff has been brought together and each one has been assigned his duty. An organization has approved the plan and furnished the funds; in return it expects progress reports, visible and quick results, and no deviation from the plan agreed upon. Everybody is happy to have a 'project,' and only Minerva covers her face and sends the owl away to catch mice. . . . If you want to prepare 200 stereoisomers of some organic compound and test their action as insecticides, a project is in order. If you want to eradicate a certain mosquito in a certain place, go and organize it. But how a major discovery or idea can come from a project I am unable to understand."—RICHARD B. GOLDSCHMIDT, *Science*, March 4, p. 219.

THE ADRENOLYTIC ACTION OF DIHYDROERGOCORNINE IN MAN

R. H. GOETZ
M.D. Berne
RESEARCH ASSOCIATE PROFESSOR OF SURGERY IN THE UNIVERSITY OF CAPE TOWN

A. KATZ
M.B. Cape Town
REGISTRAR, GROOTE SCHUUR HOSPITAL

From the Department of Peripheral Vascular Diseases, Groote Schuur Hospital, Cape Town

DIHYDROERGOCORNINE, also known as D.H.O. 180, is adrenolytic as well as sympathicolytic, an action which, to our knowledge, has never before been demonstrated in man for any ergot derivative.

In the experiments described below, the blood-pressure, peripheral blood-flow, heart-rate, respiration and skin temperature were recorded as previously described (Goetz 1949). Adrenaline 1 in 500,000 was given at a desired and constant rate with the intravenous drip (Goetz 1948), each drop being photo-electrically recorded on the plethysmogram. The investigations were made on two normal persons and three uncomplicated cases of essential hypertension—i.e., cases in which there was no evidence of congestive heart-failure, myocardial damage, disease of the kidneys or the fundi, or any other condition to which the hypertension could have been secondary.

RESULTS

Fig. 1 is a graph, prepared from a typical original film, showing the changes in blood-pressure, respiratory rate, heart-rate, digital volume and pulse volume (left first toe), all simultaneously recorded. Two doses of adrenaline 1 in 500,000, at a rate of about one drop per sec. for 2 min., were given before dihydroergocornine was administered. There were 18 drops to a millilitre, and therefore a total of about 0·000,013 g. was given, each drop containing about 0·000,00011 g. of adrenaline. The effect on the systemic circulation was practically the same for both doses: the systolic pressure rose rapidly from 130 to 160 mm. Hg while the diastolic pressure decreased by about 5 mm. Hg with the first dose and, after a small initial rise, by 10 mm. Hg with the second dose. The heart-rate advanced in both instances from about 75 to between 95 and 100 per min. The respirations increased sharply from 15 to 30 per min. in the first test and to about 22 in the second test. The vasoconstrictor effect of the adrenaline on the peripheral blood-flow is clearly shown: the digital volume decreased by about 0·2–0·25 c.cm. and the pulse volume, which before the test was 0·012 c.cm., registered 0·005 c.cm. and less at the height of the constriction. All these changes were obtained, though not so markedly, with the smallest pharmacologically effective dose of adrenaline. There was, in particular, no fall in systolic blood-pressure.

After the intravenous administration of 0·3 mg. of dihydroergocornine—which of itself caused a definite though, as in all normal persons, slight fall in blood-pressure, a respiratory depression, and in this particular case a slight rise in heart-rate—two doses of adrenaline were given at the same rate, the first 12 min. and the second about 17 min. after the administration of the ergot derivative. As can be seen at a glance, there is a well-marked change in the response of the blood-pressure to adrenaline compared with the response before the administration of dihydroergocornine. In the first test the systolic blood-pressure fell from 125 to 115 mm. Hg, followed by a slight rise to 135 mm. Hg. This dose of adrenaline, though administered at the same rate, was given for a shorter time, and therefore the total amount was considerably smaller. The effect of

Digitized by Google

this dose, therefore, may not be justifiably compared with the effects of the larger doses given before D.H.O. 180. However, in the second test the amount of adrenaline was equal to that in the two tests performed before the administration of D.H.O. 180, yet the immediate reaction of the systolic blood-pressure was a fall of about 10 mm. Hg followed by a half-hearted rise to about 10 mm. Hg above the initial level.

The change in the response of the diastolic blood-pressure was even more pronounced. In the first test after D.H.O. 180 there was a fall from about 80 mm. Hg to 65, and in the second test from 90 mm. Hg. to 60.

Fig. 2 shows the response of the systemic blood-pressure to adrenaline before and after the intravenous administration of dihydroergocornine 0·6 mg. in one of the cases of essential hypertension investigated. Before D.H.O. 180 the systolic blood-pressure responded rather abruptly, rising within less than 2 min. from 220 to 300 mm. Hg. on the administration of adrenaline 1 in 500,000 at the rate of five drops per 4 sec. for 2 min. After D.H.O. 180, which by itself caused a fall in blood-pressure from 220/120 to 150/90 mm. Hg, the systolic blood-pressure responded to adrenaline just as abruptly, but this time with a sudden drop to 110 mm. Hg. In the same patient the intravenous administration of 0·4 mg. of D.H.O. 180 did not produce this reversal of the response of the blood-pressure to adrenaline. However, it must be pointed out that the fall of blood-pressure in response to 0·4 mg. of D.H.O. 180 was rather feeble, the lowest value obtained being 180/90 mm. Hg, indicating that the dose was not sufficiently large to produce the optimum effect in this particular patient.

At this point we wish to draw attention to the prompt but gradual fall of blood-pressure in this patient on D.H.O. 180, which is typical for this drug and compares favourably with the rather abrupt response to tetraethylammonium chloride, occasionally leading to circulatory collapse.

Judging from these findings there can be no doubt that the administration of dihydroergocornine causes a definite suppression or reversal of the action of adrenaline

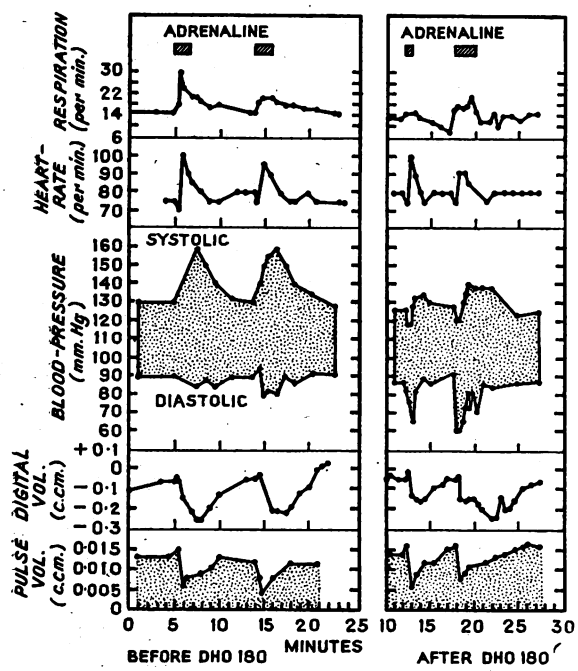


Fig. 1—Graph prepared from original film, showing effect of intravenous adrenaline before and after intravenous dihydroergocornine 0·3 mg. on respiration, heart-rate, blood-pressure, digital volume, and pulse volume (left 1st toe), all simultaneously recorded. Note suppression and partial reversal of pressor effect after dihydroergocornine.

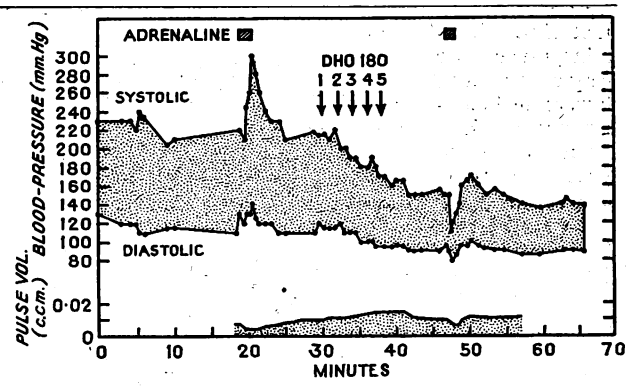


Fig. 2—Effect of adrenaline on the blood-pressure before and after the intravenous administration of 0·6 mg. of dihydroergocornine in essential hypertension. There is complete reversal of the pressor effect of adrenaline. Note also the effect of dihydroergocornine on the blood-pressure and pulse volume.

in raising the blood-pressure. However, the remaining actions of adrenaline do not appear to be interfered with. The heart-rate, as before D.H.O. 180 was given, still rose to the same degree, the respiration increased, and the peripheral blood-flow still diminished. As figs. 1 and 2 clearly show, both the digital volume and the pulse volume still responded with a decrease to adrenaline after the administration of dihydroergocornine, and this while there was a definite suppression and partial reversal in the response of the blood-pressure. This is very well illustrated by figs. 3 and 4, which show two cuttings from the original film, one being the response to adrenaline before, and the other the response after D.H.O. 180. There is no significant difference between the course of the plethysmogram after adrenaline in the two tests. In both cuttings vasoconstriction set in after the intravenous drip had been going for about 28–30 sec., leading to a fall in digital volume and pulse volume. The increase in heart-rate may be appreciated in the plethysmogram of both figures.

The effect of adrenaline on the respiration after D.H.O. 180 is worthy of comment. As already pointed out (Goetz 1949), D.H.O. 180 in otherwise non-toxic doses depresses the respiration, which may become not only very slow but also very irregular. This can be appreciated in fig. 4. With the administration of adrenaline the respiratory rate increases and, what is more striking, temporarily becomes regular while adrenaline is being given (fig. 4).

DISCUSSION

The results of these investigations are of interest not only because it has been shown that the sympathicolytic drug dihydroergocornine is adrenolytic as well, but also because our results were obtained in tests carried out on man, and not on anæsthetised animals. Dale (1913) has pointed out that the adrenolytic effect of drugs varies greatly from species to species, and Herwick et al. (1939) produced evidence that with various anæsthetics the effects might be exactly the reverse in the same animal. Results obtained in laboratory animals, therefore, may not necessarily be valid for man, and may actually be misleading.

Dale (1906), experimenting with ergotoxine, concluded that it had a specific paralysing effect on those sympathetic motor elements which are stimulated by adrenaline, the inhibitory elements retaining their normal function. Ergot paralyses the myoneural junction—i.e., the receptive mechanism of the vascular smooth muscle responding to the excitatory component of adrenaline—without influencing the receptive mechanism responding to the inhibitory or vasodilator components. Rothlin (1925, 1929), however, brought forward evidence that inhibitory functions are affected too. Nevertheless, the

Digitized by Google

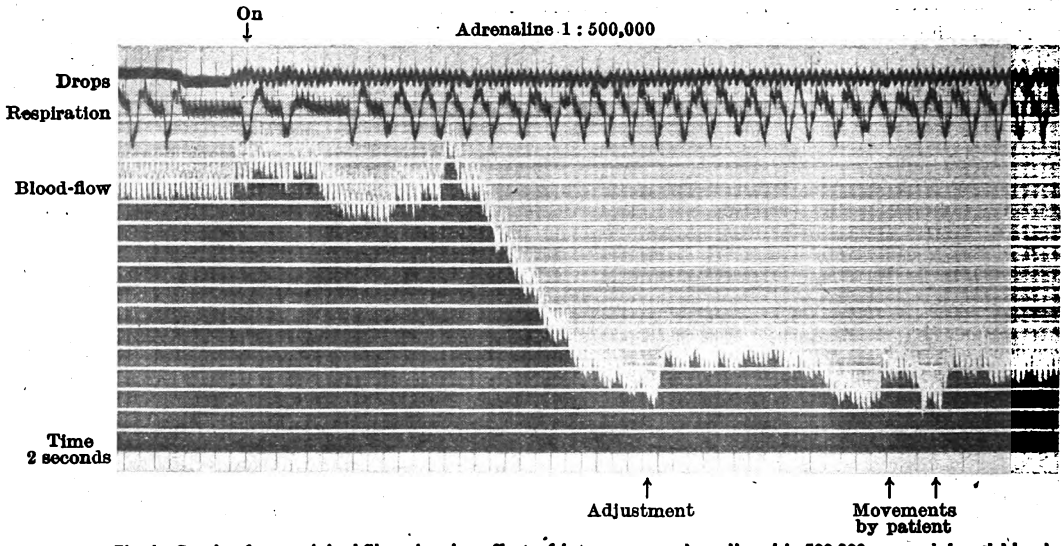


Fig. 4—Cutting from original film, showing effect of intravenous adrenaline, 1 in 500,000, on peripheral blood-flow (plethysmogram of left 1st toe) and respiration 17 min. after intravenous dihydroergocornine 0·3 mg. Same patient as in figs. 1 and 3. Note irregular breathing before and during first part of test.

fact that adrenaline, given after ergotoxine, lowers the blood-pressure has been taken as proof that there are sympathetic vasodilator fibres (Cannon and Rosenblueth 1933). It is therefore of interest that in our investigations the reversal of the pressor response to adrenaline was not accompanied by a reversal of the effect of adrenaline on the digital blood-flow. The changes in the blood-pressure response are therefore not due to changes in the dynamics of the cutaneous circulation. In any case, the blood-flow through the skin does not, it seems, account for any appreciable effect on the blood-pressure for we have repeatedly observed that the blood-pressure remains unaffected by sympathectomy of all extremities and after complete peripheral vasodilatation obtained by heating the body. The blood-pressure reversal must therefore be due to changes in the response of some other organ, possibly the muscles or the splanchnic area, and limb plethysmography with special reference to the blood-flow in muscle should throw light on this problem. Unpublished experiments on monkeys show that the blood-flow through the splanchnic area is definitely involved, inasmuch as the well-marked constrictor effect of adrenaline is completely abolished or even reversed, giving place to a dilator effect, after the administration of dihydroergocornine. Though we have not studied the cardiac output, the unaltered response of the heart-rate suggests that the heart is not involved in the reversal of the vasopressor action of adrenaline on the blood-pressure.

The investigations are also of some interest as regards the question of the existence of sympathetic vasodilator fibres in man. The fact that D.H.O. 180 does not interfere with the peripheral vasoconstrictor action of adrenaline suggests that there are no sympathetic vasodilator fibres supplying the vessels of the digits in man. Should it be argued that the dose of D.H.O. 180 was perhaps insufficient to unmask the existence of such fibres, we should have to point out that, after all, the dose did reverse the blood-pressure effect of adrenaline in our cases.

Dihydroergocornine apparently does not promote the destruction of adrenaline in vitro. It has been possible to test the activity of a mixture of adrenaline with dihydroergocornine and to compare the results with control solutions in which adrenaline alone was given at the same rate. There was no difference in the response of the blood-pressure in these tests.

The recognition of the adrenolytic action of D.H.O. 180 in man, in addition to its already known sympathicolytic action, may be of considerable importance as regards the possibilities offered by this drug in the management of disturbances of the autonomic nervous system, especially in view of the fact that after other sympathicolytic drugs, such as tetraethylammonium chloride, a hypersensitivity to adrenaline has been reported. The cases are legion in which there is a disturbance

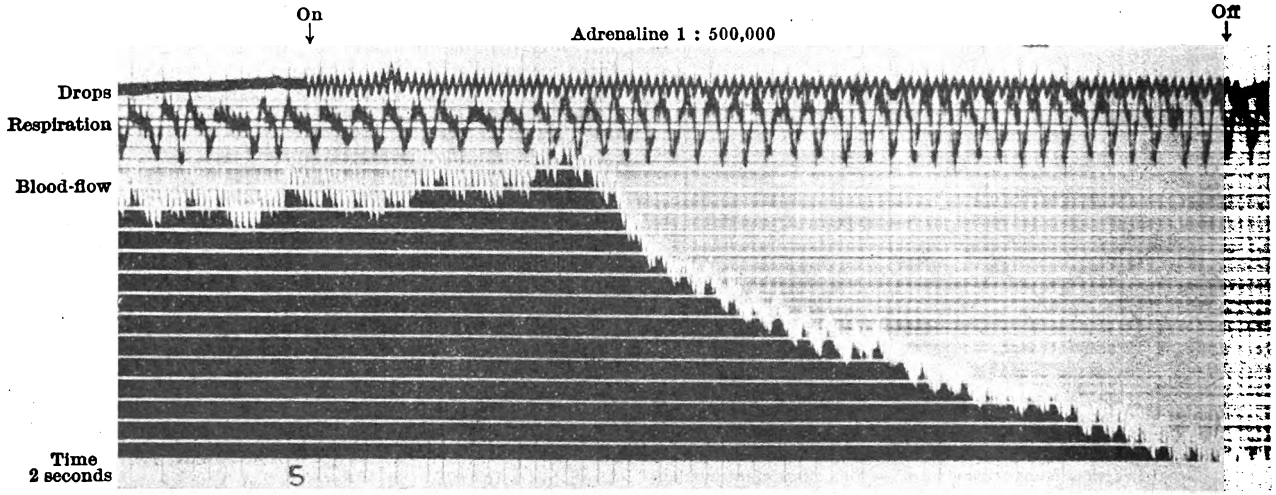


Fig. 3—Cutting from original film, showing effect of intravenous adrenaline, 1 in 500,000, on peripheral blood-flow (plethysmogram of left 1st toe) and respiration before administration of intravenous dihydroergocornine 0·3 mg. White horizontal lines = calibration for plethysmogram = 0·01 c.cm. from one line to the next. Same patient as in figs. 1 and 4.

Digitized by Google

of either the central or the peripheral reflex proprioceptive regulatory function of the sympathetic nervous system, neurogenic hypertension being but one example, and a drug which has both sympathicolytic and adrenolytic properties may have an important rôle in the management of these disorders. It should be interesting to see the effect of D.H.O. 180 on the blood-pressure in conditions and circumstances characterised by an outpouring of adrenaline—e.g., the presence of a pheochromocytoma.

SUMMARY AND CONCLUSIONS

Dihydroergocornine, besides being sympathicolytic, suppresses and reverses the pressor response to adrenaline in man. It does not, however, abolish the cardio-accelerator effect of adrenaline.

The vasoconstrictor effect of adrenaline on the digital circulation is not affected by dihydroergocornine given in doses sufficient to suppress or reverse the effect on the blood-pressure.

The stimulating effect of adrenaline on the respiratory centre (direct or indirect) is not abolished by doses of dihydroergocornine sufficient to reverse or suppress the pressor response. The respiratory depression produced by dihydroergocornine is abolished, and respiration is regular, while adrenaline is administered.

Dihydroergocornine apparently does not promote the destruction of adrenaline either in vitro or in vivo.

The possible clinical usefulness of dihydroergocornine is indicated.

These investigations were made possible by the courtesy of Prof. E. Rothlin, of the Sandoz Research Laboratories, Basle, Switzerland, who provided the dihydroergocornine, and were aided by a grant received from the South African Council for Scientific and Industrial Research. To Miss L. Commins and Mr. C. C. Goosen we are indebted for valuable technical assistance both during the experiments and in the preparation of the graphs.

REFERENCES

Cannon, W. B., Rosenblueth, A. (1933) *Amer. J. Physiol.* **104**, 557.
Dale, H. H. (1906) *J. Physiol.* **34**, 163.
— (1913) *Ibid*, **46**, 291.
Goetz, R. H. (1948) *Lancet*, **i**, 830.
— (1949) *Ibid*, March 26, p. 510.
Herwick, R. P., Linegar, C. R., Koppanyi, T. (1939) *J. Pharmacol.* **65**, 185.
Rothlin, E. (1925) *Klin. Wschr.* **4**, 1437.
— (1929) *J. Pharmacol.* **36**, 657.

REABLEMENT OF TUBERCULOUS PATIENTS

R. GRENVILLE-MATHERS
M.A., M.D. Camb., M.R.C.P., F.R.F.P.S.
CONSULTANT TUBERCULOSIS OFFICER, WALLASEY, CHESHIRE

IT is now recognised that the treatment of the tuberculous patient is not complete until he is once again an economic unit employed in a situation which is not deleterious to his condition. Fulfilment of this is difficult, since there is always a doubt about the stability of any lesion, and the disease restricts working capacity without necessarily impairing mental and physical functions.

It was formerly usual to advise the patient with tuberculosis to return to his former occupation, since it was regarded as less strain for him to do the work to which he was accustomed than to attempt an entirely new occupation in strange surroundings. Often, however, the nature of the employment is a factor in the production of the original breakdown.

For those not considered fit to resume their previous occupation the village settlement has been regarded as a sine qua non. However desirable such settlements may be in theory, they are only taken advantage of by a minute number. Patients and their families are reluctant to live in a colony, often far from their usual districts and friends. In consequence attempts to start new settlements have not been successful, and the last report of the British Legion Village (1945–46) shows that the existing schemes are not an unqualified success.[1]

Reablement is only capable of complete fulfilment if full employment is maintained. When there are able men and women unemployed, employers will not attempt to move employees from one job to another in order to employ a disabled person. This reluctance on the part of the employers to use disabled persons is shown by the way in which the demand for sheltered employment increases as the general level of unemployment rises.

WALLASEY RESETTLEMENT CLINIC

Wallasey is a county borough with a population of 104,000. It is mainly residential, its principal industries being flour-milling, engineering, and belt manufacture. It is a part of Merseyside, which has a variety of occupations; but all jobs outside Wallasey involve a long time spent in travelling. Unemployment is very high. In April, 1948, there were 936 men and 470 women registered as unemployed in Wallasey, and 20,788 men and 4731 women unemployed on Merseyside. Nevertheless, of 375 men and women on the dispensary register with pulmonary tuberculosis 65% are employed.

We have a resettlement clinic where crafts and occupations are taught by a qualified teacher supplied by the corporation's education committee. This clinic is for outpatients, but a few inpatients attend from the sanatorium. The disablement resettlement officers of the Ministry of Labour attend this clinic, and discussions are held about the various patients deemed fit for employment.

In deciding which occupations to allow a patient with pulmonary tuberculosis to follow we have had recourse to the Registrar-General's decennial supplement for England and Wales, 1931, dealing with occupational mortality. The ten occupations with the highest standard of mortality-rates for pulmonary tuberculosis are as follows:

Tin, copper, and underground metalliferous mine workers
Sandblasters
Grinders
Glass blowers and finishers
Pottery dippers, glazers, painters, and decorators
Stevedores
Glazers, polishers, chuffers, and moppers
Kiln and oven men
Hat formers, plankers, and stiffeners.
Slate workers.

The occupations with mortality-rates for pulmonary tuberculosis above the average of the whole population are as follows:

Barmen
Boiler scalers
Boiler makers, platers
Boot and shoe makers and repairers
Brass and bronze labourers
Brass finishers and turners
Cabinet makers
Cigarette makers
Clerks and typists
Compositors
Coopers
Costermongers
Cutlers
Dock labourers
Dress makers and cutters
File cutters
Filers
Foundry labourers
French-polishers
Furnace men
Glove makers
Hoop makers
Horse drivers
Hotel porters
Labourers (general)
Laundry workers
Masons
Messengers and porters
Metal grinders
Metal machinists
Metal moulders and casters
Musicians
Newspaper sellers
Paperhangers and decorators
Press workers and stampers
Printers
Puddlers
Riveters
Seamen
Snuff workers
Solderers, braziers, and tinners
Stationery and cardboard-box makers
Stone workers
Textile goods makers
Waiters
Watchmen
Wire and tube makers

No person, unless his lesion is already quiescent, has been recommended to return to any of the occupations listed above except clerks, typists, dock labourers, and watchmen.

DOCK WORKERS

Clerks, typists, and watchmen follow sedentary occupations, and it has been felt that, provided working

1. *Tubercle*, 1948, **29**, 47.

Digitized by Google

conditions are suitable, they should be allowed to continue in these occupations. In a port area registered dock workers, by their numbers, constitute a special problem.

Normally a dock worker works on "full guarantee," which means that he must report eleven times a week at control, when he can be directed to work day or night. Normally day work is from 8 A.M. to 12 noon, and 1 P.M. to 5 P.M. Very often work is continued to 7 P.M. There is a week of five and a half days, and some Sunday work consisting of a six-hour day is done. The night shift begins at 11 P.M. and lasts until 7 A.M. and operates six nights a week.

Such employment is too heavy for most patients with pulmonary tuberculosis, but reduced hours of work are possible by means of what is called "reduced guarantee." The reduced guarantee on Merseyside is for "six turns" (a "turn" is a period of four hours), and a man must report at the control each morning at the nominated time. If, however, he is not engaged at the morning call the "six turn" man need not attend the midday call. A "six turn" man is not put on night work or Sunday work. Once he starts work, however, he works the same hours as the other men. Thus in selected cases night work and Sunday work can be prevented simply by placing a man on a "reduced guarantee," and to do this the coöperation of the medical officer and the executives of the National Dock Labour Board has been readily available.

Observations of the different types of work available to the registered dock workers suggest that the following do not involve strenuous work:

Landing man	Scribers
Truck driver	Guy man
Hatch man	Markers
Winch man	Deck hands
Checker	

Visits to other industries arranged by the Ministry of Labour also showed that each contained occupations which could be undertaken by disabled persons.

PHYSICAL INDEX

Brieger [2] tried to reduce the assessment of the working capacity of tuberculous patients to the exactitude of a laboratory report; but his assessments are long and time-consuming and are unsuitable for use in an ordinary resettlement clinic. A modification of this scheme has been devised and used in making reports to the Ministry of Labour on form D.P.IX. The index consists of a prognostic index (maximum 50 marks), a respiratory and circulatory index (20 marks), a work index (10 marks), and a home index (20 marks).

PROGNOSTIC INDEX

	Marks
Disease arrested	50
Disease quiescent	48
Lesion controlled by collapse therapy	45
Lesion regressive, sputum negative	42
Lesion unilobular; regressive; sputum converted	40
Lesion multilobular; regressive; sputum converted	35
Fibrotic lesion; occasional positive sputum with intervening negatives; lesion almost unilateral; weight steady	30
As above but lesion bilateral	25
Sputum positive; amount of sputum small; weight steady	20
Fair chronic; sputum positive; sputum 1 oz. or more; weight steady	15
Fair chronic; as above but weight unstable	10
Bad chronic; large amount of sputum; temperature and weight unstable	2

RESPIRATORY AND CIRCULATORY INDEX

Resting pulse-rate:

60–70	6 marks	85	3 marks
75	5 „	90	2 „
80	4 „	95	1 mark

Time for which breath can be held:

50 sec.	6 marks	30 sec.	3 marks
40 „	5 „	20 „	2 „
35 „	4 „	10 „	1 mark

Time taken for pulse-rate to return to normal after standing on chair and stepping down ten times:

1 min.	8 marks	5 min.	3 marks
2 „	6 „	6 „	2 „
3 „	5 „	7 „	1 mark
4 „	4 „		

2. Brieger, E. Papworth Research Bulletin, 1938.

WORK INDEX

Patient can lift

7 lb. for 5 min. .. 5 marks 7 lb. for 2 min. .. 2 marks

Time taken for pulse-rate to return to normal after five minutes' work:

3 min.	5 marks	6 min.	2 marks
4 „	4 „	7 „	1 mark
5 „	3 „		

Time taken for pulse-rate to return to normal after two minutes' work:

3 min. .. 2 marks 5 min. .. 1 mark

HOME INDEX

Good home .. 20 marks Poor home .. 5 marks
Fair home .. 10 „

EMPLOYMENT REGISTER

The employment register for tuberculous patients has been analysed in the light of the work of the resettlement

TABLE I—EMPLOYMENT REGISTER OF 225 MALES

State of employment	No. of cases	Home conditions			Number in each stage of disease (Memo 37/T)				Number still sputum-positive
		Good	Fair	Poor	A	B1	B2	B3	
Employed ..	147	90	46	11	54	12	75	6	35
Unemployed ..	11	4	6	1	3	0	8	10	1
Unfit	32	14	10	8	3	0	24	5	27
In sanatorium or waiting admission ..	35	Unclassified							

clinic. The numbers have been broken up for both men and women according to the Ministry of Health's classification (memo 37/T) on diagnosis. In addition, the patients have been classified by the health visitor according to whether their home conditions are good, fair, or poor. This classification has not been related to the amount of money available, the quality of the furnishings in the house, or the neighbourhood in which the house is situated, but to the care and attention given to the patient in the home, to whether the money available is spent wisely, and to whether the patient can get proper rest.

Men.—Table I shows the number of men employed, unemployed, not fit for work, and in, or awaiting admission to, sanatorium. Altogether 65% are working and 20% in, or awaiting admission to, sanatorium. Of 63 men who are still "sputum-positive" 55% are working. Of 67 men who are "sputum converted" 86% are working. Of 60 men who are "sputum-negative" 90% are working. 5% are unemployed and 14% unfit for work. This last group includes men who would be fit for employment under sheltered conditions but are unsuitable for the open labour market.

Women.—Table II is a similar classification for women. If those employed and doing housework, which means that they are doing the same amount of work in the house as before they fell ill, are grouped together, 66% are working. Of 31 women still "sputum-positive" 58% are working. Of 47 women "sputum converted" 89% are working. Of 43 women "sputum-negative" 93% are working. 4% are unemployed and 10% unfit for work.

DISCUSSION

The tables show that a large proportion of persons with pulmonary tuberculosis are capable of working in industry on normal terms.

Analysis of the employment tables shows no single factor which determines employability. The presence of a positive sputum reduces the proportion employed, but

Digitized by Google

55% are in employment, and 10% of those who have never had a positive sputum are unfit for work. This is therefore not an overriding factor. The reablement index has not been found to constitute a better criterion for employment than a general assessment of the patient carried out by the physician who has treated him. The usefulness of this index lies only in the guidance it gives to non-medical officers of the Ministry of Labour. This finding confirms the old adage that the tuberculous patient is a law unto himself. Fitness for any occupation cannot be defined by physiological measurements alone. All men are individuals and it is impossible to bring about uniformity.

Such a conclusion emphasises the need for the patient to be under the care of one physician from the time he is diagnosed until he is taken off the register with his lesion healed. In no other way can a sufficient knowledge of the behaviour of the pulmonary lesion and of the patient's psychological make-up and capabilities be obtained.

Reablement should begin as soon as the patient is fit for graduated exercises. From this time the period spent in a sanatorium workshop should be gradually increased. After discharge from the sanatorium he should continue to attend the workshop and then graduate to employment under sheltered conditions. From here many can eventually enter ordinary industry. Such factories affording sheltered employment should be based on populations of about 250,000 so that they are within easy reach of the whole area. In this way complete reablement can be achieved without much need for disturbing the family life of the disabled person. Such a process also means that the patient is not kept idle for a long time. A patient kept idle too long is apt to become introspective and neurotic or lazy and unemployable.

Finding employment for these people could be much easier if the proportion of disabled persons who have to be employed could be raised, especially where there are more than 100 employees, since it has been found that many employers had the present 3% of disabled persons on their staffs without engaging new employees. Secondly,

TABLE II—EMPLOYMENT REGISTER OF 152 FEMALES

State of employment	No. of cases	Home conditions			Number in each stage of disease				Number still sputum-positive
		Good	Fair	Poor	A	B1	B2	B3	
Employed ..	43	26	15	2	17	2	24	0	5
Housework ..	57	40	12	5	23	3	28	3	13
Unemployed ..	6	2	2	2	2	1	3	0	0
Unfit	15	10	4	1	1	0	7	7	13
In sanatorium or waiting admission ..	31	Unclassified							

the scheduling of employments reserved for disabled persons ought to be done on a regional, rather than a national, basis. At present the only occupations so scheduled are lift and car-park attendants. In this area there is only one public lift, and the occupation of car-park attendant is seasonal. Hence the present schedules have been of little help. Thirdly, both local and central government offices have many jobs eminently suitable for disabled persons, but neither will employ persons with tuberculosis. At a time when the number of persons employed by these two bodies is growing they should lead the way by employing more disabled persons.

SUMMARY

The work of a resettlement clinic in obtaining employment for patients with pulmonary tuberculosis is described.

Of 375 patients on a dispensary register 65% are in employment.

A simple physical-efficiency index has been devised whose main use is in guiding non-medical officers of the Ministry of Labour.

No one factor determines employability of tuberculous patients. Each patient must be considered as an individual.

I wish to thank Dr Ronald B. Berry, M.O.H.; Miss A. Glassey, tuberculosis health visitor; Mrs. H. Gorst, Mr. F. Gaultness, and Miss C. Flenley, of the Ministry of Labour; and Dr. E. Holland and Mr. E. Fox, of the National Dock Labour Board, for all their help.

CRETINISM WITH GOITRE IN INFANCY

TWO CASES TREATED WITH THYROID

VICTORIA SMALLPEICE

M.D., M.R.C.P., D.C.H.

PHYSICIAN, CHILDREN'S DEPARTMENT, RADCLIFFE INFIRMARY, OXFORD

THE administration of thyroid to young children with cretinism and goitre may have very satisfactory results as regards both the swelling in the neck and the physical evidence of hypothyroidism. As in all cases of cretinism, mental progress is unpredictable.

The higher incidence of cretinism in areas where goitre is endemic has long been recognised. Though in certain endemic regions the two may appear together in infancy, in others the combination is uncommon.

McCarrison (1917), working in India, recorded that he had seen only 2 cases of goitre before the age of 3 years in 203 cretins. The association is rare in sporadic cretinism. Rienhoff (1940) reports 2 cases in sisters aged 16 and 18 years, who were born in a non-goitrous area of the United States. The father was Swiss; he had a goitre, and both his parents were affected. The two patients were said to have had large goitres since birth, associated with hypothyroidism. Both had been treated with large doses of iodine for two years, during which time the goitres had increased. When treated by Rienhoff with thyroid by mouth they lost their hypothyroidism, and after six months' treatment there was no visible evidence of goitre in either case. Rienhoff also reported the case of a newborn baby with severe dyspnœa and cyanosis produced by pressure from a large goitre. Following his experience in the earlier cases he gave a hypodermic injection of thyroxine, and the symptoms were relieved in a few days, with obvious reduction in the size of the thyroid gland. He does not give the subsequent history nor indicate whether cretinism was present in addition to the goitre. He also reports disappearance of a goitre in a boy, aged 11 years, with hypothyroidism, in whom the swelling had been noticed at the age of $2\frac{1}{2}$. When thyroid treatment was stopped temporarily, the gland enlarged again.

The following 2 cases are presented in detail because of their unusual features.

CASE-RECORDS

Case 1.—A cretin aged 8 months presented in August, 1942, with dysphagia and stridor associated with a soft-tissue swelling (probably composed of abnormal thyroid tissue) in the neck. The family doctor referred her because he had been called two days earlier on account of her noisy breathing and difficulty in swallowing. He reported that she had been taking small unspecified doses of thyroid.

The mother, Mrs. A., an Austrian refugee, was born at Erlach, fifty miles from Vienna; she is one of three sisters, who are said to be well. She came direct to Gloucestershire at the age of 21. On her marriage at the age of 23 she went to live in Berks. Her mother, who remained in Austria, has a goitre and is said to be the only case in a family of ten. Though unaware of it, Mrs. A. had a symptomless slight generalised enlargement of the thyroid. During pregnancy she had had no extra vitamins, and fish supply had been irregular, but diet had otherwise been good; apart from slight morning sickness throughout, her health had been excellent.

Digitized by Google

The patient's father is English, and his mother, who lived near them, "had a big goitre but was quite well." The patient's sister, 18 months older, is said to be normal.

Past History.—Full-term normal labour; birth-weight 9 lb. She did not cry at birth and, at the age of 1 month, was first taken to a doctor because she was not thriving. At 3 months she had pneumonia, and immediately after this was referred to an ear, nose, and throat surgeon because of stridor. At this time she was seen by a pædiatrician, who started thyroid treatment; but no record of the consultation can be found, and the child's progress was not followed. This history was obscured at the time by the language difficulty and the fact that there had been two changes of family doctor.

Examination.—The baby appeared mentally backward, though no specific abnormality was recognised. She was overweight (23 lb.); the general condition was fairly good. The anterior fontanelle was widely open; muscle tone was poor, and there was a small umbilical hernia. The whole picture was dominated by the curious signs of obstruction. The baby held her head thrown back, and there was inspiratory stridor with frequent choking, more obvious on attempting to swallow. There was no evidence of retropharyngeal abscess or of intrathoracic lesion; the neck was short, palpation was difficult, and no definite mass could be detected. On the whole, disease of the cervical spine appeared to be the most likely diagnosis, and she was referred for radiography of that region in the belief that admission to an orthopædic hospital might be indicated. The radiologist reported "soft-tissue swelling behind the trachea and larynx; pharynx displaced forward. This seems to explain the respiratory difficulty. Chest nil abnormal" (fig. 1).

The family lived in a remote village, and in spite of a second letter the child did not attend again until sent up by yet another doctor a year later, at the age of 1 year and 8 months. On this occasion the difficulty in swallowing and the stridor were unchanged, but the mental and physical backwardness was more evident. She was pale and hypotonic, with well-marked kyphosis; the fontanelle was closed, but the head circumference was $19\frac{1}{2}$ in.; the umbilical hernia had disappeared. She had only started to crawl in the previous week and could not sit up without support; she could not talk. Constipation was severe, and blood was present in the stools. The picture was now one of definite cretinism, with pressure symptoms from a soft-tissue swelling in the neck. Radiography again showed the tracheal deformity, though it was rather less. The long bones showed some suggestion of delayed ossification. There was a deformity of the spine such as is seen in cretinism.

It was thought wise to admit the child for observation and to treat the cretinism before further investigation of the dysphagia and stridor. She was given vitamin D 1400 units daily together with iron; thyroid was started in doses of gr. 1 daily and increased to gr. 2 after a month. Her physical appearance rapidly improved, and after 3 weeks in hospital she was trying to talk. By the end of the first month she was standing and having much less difficulty in swallowing. After 2 months she was feeding herself, taking all food normally, and both dysphagia and stridor had disappeared. Dr. F. H. Kemp reported on the barium swallow: "I am afraid it is just impossible to obtain a film. No abnormality seen as far as one can recognise." Subsequent films confirmed this (fig. 2).

The family has since left the neighbourhood. When seen at the age of 4 years 4 months the patient showed no evidence of cretinism or of her early dysphagia and stridor, though there was some nasal obstruction from adenoids. Her height, which had been 3 in. below average at the start of treatment at 1 year and 8 months, was now only $\frac{3}{4}$ in. below the average. Her skeletal maturity was advanced, and when she was only 3 years and 8 months old had reached that of 7 years and 3 months. Her mental progress had been very disappointing; she did as she was told, fed herself, and tried to dress herself, but her appearance was definitely abnormal as regards intelligence. Miss Grace Rawlings reported "chronological age 4·4, mental age under 2. This child is a mental defective." At one period her dose of thyroid had been pushed to the limit of tolerance without any mental improvement, and it seems unlikely that there will be any further progress in this direction.

Case 2.—A child in whom a goitre had been noted at birth was first seen in Febuary, 1947, at the age of 1 year and 11

Fig. 1—Lateral view of neck of case 1, showing deformity of trachea, larynx, and pharynx before treatment.

Fig. 2—Lateral view of neck of case 1, showing normal contour after treatment.

Digitized by Google

months because of swelling of the neck since birth and general backwardness.

There was no history of thyroid abnormality or goitre on either side of the family and social conditions were satisfactory; the father, aged 32, was a miller's foreman, and they had a five-roomed house with indoor sanitation in an Oxfordshire town. The mother was 22 years old at the birth of this, her first, child. The infant was postmature. The mother was admitted to hospital as an emergency for protracted labour and contracted outlet, and a lower segment cæsarean section was performed.

The child's birth-weight was 11 lb. A swelling was noted immediately after birth. It was soft, about $1^1/_2$ in. across, the greater part to the right of the trachea but with a lesser portion to the left; it was in the position of the thyroid gland and attached to the trachea; it did not transilluminate and was thought to be a cystic enlargement of the thyroid. The child was seen by Mr. D. C. Corry at 8 days old and kept under observation in the surgical clinic.

Fig. 3—Case 2, aged 2 years, showing cretinism and goitre before treatment.

When the baby was 5 months old, in August, 1945, a different observer thought the swelling had disappeared, and discharged the baby from hospital. When the mass appeared to be growing more rapidly, the mother asked for another appointment and, at 1 year and 7 months, the baby was seen again and put on Lugol's solution, 1 minim daily, without any improvement. He had been breast-fed for six months, and there had been no feeding difficulties; first tooth at 11 months; sat up at 9 months. His general health had been excellent.

On examination at 1 year and 11 months he could not walk alone or talk; weight 28 lb.; height 2 ft. 6 in. ($2^1/_2$ in. below average). He was a stout friendly child with thick short neck, and his limbs were short in proportion to the trunk (fig. 3); the fontanelle was closed; abdomen protuberant. The expression, skin, and complexion suggested hypothyroidism. There was a soft diffuse enlargement of the thyroid gland, with a firm mobile mass about 1 in. in diameter in the right lower pole. He was admitted to hospital for further investigation and to observe the effect of thyroid therapy on both the cretinism and the goitre.

Radiography at 2 years showed skeletal age 0–3 months, and changes compatible with hypothyroidism. Blood-cholesterol 307 mg. per 100 ml.; red cells 4,300,000 per c.mm., Hb 82%, colour-index 0·95.

He began thyroid treatment on March 1, 1947, first taking gr. $^1/_2$ b.d., and in a few days this was increased to three times a day. A month later both the diffuse swelling and the nodule were much smaller. After a further 2 months on treatment, when he was 2 years and 3 months old, the thyroid was no longer visible (fig. 4). The nodule could still be palpated though considerably smaller in size. Skeletal age at this time had increased to about 1 year (a very rapid change).

When last seen at 2 years and 9 months he appeared to be progressing satisfactorily. The goitre was not visible, and the nodule was now difficult to palpate and was about $^3/_8$ in. in its greatest diameter. He was on gr. 2 of thyroid daily, but in view of the fact that his pulse-rate had risen to 120 per min. the dose was reduced to gr. $1^3/_4$. Miss Rawlings had examined him the previous month and reported: "This child's intelligence is now between the 18th month and the 2nd year level of development." He is remaining under treatment. The sib, born in January, 1947, is normal.

DISCUSSION

The two cases described appear to represent different clinical pictures of a process which is fundamentally similar. Both children are undoubtedly cretins whose physical signs of cretinism responded rapidly to adequate thyroid therapy. Biopsies of the thyroid glands were not obtained, but consideration of other work throws some light on these cases. Eaton (1945) reported a female child in whom the entire thyroid outline was visible at birth following treatment of the mother with thiouracil during pregnancy; in this case once the infant started its independent existence it rapidly became normal. Hughes (1944) had produced a similar condition in young rats after treating the adult female with thiouracil for eight months before parturition. Astwood et al. (1943) showed that administration of certain sulphonamides or of thiourea to rats gave rise to thyroid hyperplasia, which they considered compensatory; they believed that the drugs prevented the thyroid gland from synthesising thyroxine, and that the resulting low blood-thyroxine level caused the anterior pituitary to increase its secretion of thyrotrophic hormone; this in turn caused thyroid hyperplasia. The hyperplastic goitre thus produced was accompanied by hypothyroidism; both could be abolished by administration of thyroid or by hypophysectomy but not by large supplements of iodine. These observations taken together give some indication of the manner in which hyperplastic goitre might be present at birth, when the mother's thyroid function is upset, or goitre and hypothyroidism might appear later due to some sequence of events such as Astwood et al. have described. The condition so well seen in case 2, in which sporadic cretinism and goitre were present together at birth and persisted until thyroid was administered, is a far more complex problem, and the ætiology remains obscure.

Fig. 4—Case 2, aged 2 years and 3 months, showing that goitre is no longer visible. Child is wearing shirt which fitted him before treatment.

In case 1 the story and the subsequent progress suggest that the soft-tissue swelling responsible for pressure symptoms was a goitre. Dr. Kemp tells me he has recently radiographed a healthy child whose pharynx showed a change of contour midway between the normal and that of case 1 before treatment. Nevertheless the simultaneous regression in the signs of cretinism and in the pressure symptoms, together with the radiological change, point to the fact that all three were associated, and that thyroid therapy caused the rapid improvement. It seems possible that the gland had originated in its normal position and extended backwards to occupy the unusual site shown by X rays.

In view of the result obtained in case 1, a similar sequence of events was predicted when thyroid was administered to case 2. Here the picture was clear-cut. The goitre was in the usual site, and observations on the effect of treatment could readily be made, though its very soft consistence made accurate measurement difficult. Unlike case 1, he had had no thyroid treatment, so the picture was not masked in any way. He had been taking iodine for several months without improvement. Finally the fact that the skeletal age at 1 year and 11 months was only 0–3 months suggests that cretinism had been present since birth. Bartels (1945) has drawn attention to the possibility of spontaneous return of thyroid function, or even hyperthyroidism, in a cretin

Digitized by Google

where an adenomatous goitre is present. The small nodule still present in the region of the right lower pole in case 2 makes this a possibility to be borne in mind.

SUMMARY

Two cases of cretinism are described.

In both a soft-tissue swelling was present in the neck. In case 1 this was not palpable but was demonstrated in lateral X-ray films of the region and was associated with pressure symptoms. In case 2 the mass was easily identified as due to thyroid enlargement.

In both cases symptoms of cretinism and signs and symptoms due to the mass regressed rapidly on administration of thyroid.

I am indebted to Mr. D. C. Corry, surgeon to the Radcliffe Infirmary, Oxford, who referred case 2. Dr. F. H. Kemp, radiologist to the hospital, kindly supplied the X-ray photographs and reports, and Miss Grace Rawlings investigated the mental development of the two children.

REFERENCES

Astwood, E. B., Sullivan, J., Bissell, A., Tyslowitz, R. (1943) *Endocrinology*, **32**, 222.
Bartels, E. C. (1945) *Surg. Clin. N. Amer.* **25**, 672.
Eaton, J. C. (1945) *Lancet*, i, 171.
Hughes, A. M. (1944) *Endocrinology*, **34**, 69.
McCarrison, R. (1917) The Thyroid Gland in Health and Disease. London; p. 122.
Rienhoff, W. F. jun. (1940) *Arch. Surg.* **41**, 487.

Medical Societies

ROYAL SOCIETY OF MEDICINE

Specialisation

A MEETING of the section of medicine on March 22, with Sir ADOLPHE ABRAHAMS, the president, in the chair, was devoted to a discussion on the Value and Abuse of Specialisation.

Sir ROBERT YOUNG suggested that the chief factors promoting specialisation had been: (1) the development of instrumental methods; (2) the ample gifts of science applied to medicine, as witnessed in physiology, pathology, biochemistry, and biophysics; and (3) public demand, often fostered by the lay press, for special knowledge and skill. Among the possible misuses of specialisation was a direct approach by the patient to the specialist. In this respect the law managed its affairs better, for here the specialist must be approached through a solicitor. Sir Robert looked now to the health centre to supply the patient with everything he needed; and control of investigations and treatment should remain with the general practitioner.

"I fear," he continued, "that we are witnessing the passing of the general physician." The student was taught by specialists, who were also enthusiasts; but the methods of the older physicians should not be cast aside, for a full routine examination might make clear what form of specialist attention was needed. He was convinced that training by the general physician produced the best type of general practitioner; and he hoped that when the pendulum of change had completed its present swing, some future Minister of Health would ask medical schools to revive teaching of the old type, whereby the student's eye would be fixed, not on the work of a special department, but on the make-up of the patient. The practitioner was nowadays involved in a vortex of paper; he must be freed from this to have the unharried and unhurried care of his patients. Finally, patients must be protected from the myopic outlook of the ultra-specialist.

Mr. A. DICKSON WRIGHT forecast the appearance of a great rash of specialists, with at least temporary eclipse of the general science of medicine and surgery. Already, he said, the general practitioner had rather lost his position in public esteem. Yet the specialist system should be integrated with a good general-practitioner system. In the U.S.A., where development of the specialist system had gone further than in Britain, the practitioner was obscured; and now patients drifted from one specialist to another like a ship without a rudder.

To the patient there were particular dangers today, when specialists were no longer well grounded in general medicine and surgery. People would no longer submit to an overhaul by a person they had learned to despise—the practitioner. Nevertheless the practitioner might still play a vital rôle, as the following case showed:

A Service patient had a carbuncle on the face, which healed. Subsequently a pleural effusion developed, and he was admitted to a thoracic unit where detailed investigations of the respiratory system were made, all with negative results. Operation was contemplated, but the patient's practitioner managed to extract him from the unit, and sent him to a general surgeon who drained a perinephric abscess.

Mr. Dickson Wright went on to say that the prospective specialist could not afford, after qualifying, to dally wi h general medicine or surgery; for thus he would fall behind in the race for appointments, and if he persisted in this dalliance he would be considered second-rate by his colleagues and by the public. In the teaching hospitals the narrow specialist often thought his own work too advanced for undergraduate students; and thus, though he might be an excellent teacher, his services were lost to the student, who was taught by the few remaining general physicians and surgeons. About specialists there was a certain exclusiveness: the general physicians and surgeons were being rather left behind in prestige, although they carried the real burden. Fortunately, however, there were already signs of a movement towards melting back a number of specialties into the general sphere.

As to abuses, the specialist might become bored by the monotony, and worried by the narrowness, of his field. Then he might—as some indeed were already doing—expand into adjacent territory. For example, one day the thoracic surgeon might find that a number of interesting things passed through his cavity; these tissues, like the Polish corridor, were not now his concern, but if he made them so he would be led into a number of other fields. Secondly, Mr. Dickson Wright deplored the tendency of specialties to become narrower, and he particularly decried specialisation by diseases. He also had a word for the ultra-specialist, who engaged in over-elaborate examinations, often wrapped up in ritual; of gastroscopes he said, "I hope I'll never see one pointed at me."

Specialisation was having a bad effect on the public and on students; and general practice was commanding fewer and fewer good men. He believed, however, that many of the evils would be overcome if recruitment to the specialties were deferred to allow of grounding in general medicine and surgery.

Sir HENRY COHEN pointed out with regard to research that the narrower the field the deeper it was possible to dig. As to undergraduate training, the teaching hospitals sometimes contained a great deal of unsuitable material; the student might spend several months in a surgical ward without seeing an instance of some of the commoner disorders such as hernia and whitlow. The teacher of undergraduates should aim at inculcating a philosophy of medicine; one teacher should demonstrate how the principles of medicine can be translated in terms of clinical medicine, wherever in the body disease manifests itself.

Every patient who was ill should consult a general practitioner, who ought to have a general training. Sir Henry Cohen argued that the practitioner should have at his disposal the assistance of specialists—such as radiologists and clinical pathologists—who could give him any diagnostic or therapeutic help that he required. But when there remained difficulties in diagnosis or treatment he should also be able to refer patients to a consultant. The consultant, whatever his special interests, must be primarily an experienced general physician. He in turn might refer the patient to one or more specialists, and his job was to synthesise the information thus obtained. Whereas from some specialists the practitioner sometimes got the unsatisfactory reply that "there is nothing wrong in my department," the consultant should be able to express a positive opinion.

One danger of specialisation was that the specialist so often discovered, and insisted on treating, disorders in his own department unrelated to the patient's com-

Digitized by Google

plaint. Sir Henry quoted as examples of such disorders focal sepsis, gastroptosis, displacements of the uterus, and chronic cholecystitis. Moreover, specialists might become so technically competent in a certain procedure that they took a pride in the performance of it, without questioning the need. Then again, man was more than the sum of his parts; no one system could be isolated from another. Certain specialties were justified—for instance, surgery and some of its branches, where craftsmanship improved with practice. Specialisation was also justified where the conception of the whole patient was retained—as in pædiatrics and geriatrics. But specialisation on the basis of a diagnostic or therapeutic machine was never justifiable. Students, he concluded, should be trained in the general concepts of medicine as an indispensable basis for any later specialty.

In the course of the discussion, Dr. MAURICE DAVIDSON urged that, as in the last century, the student should receive at the university a more general education. For some years he had felt that the responsibility for present deficiencies lay at the top. In the last twenty-five years the medical committees of the great teaching schools had tended to make appointments on the score of prominence in a narrow field. The question "what has he done?"—meaning what research—had replaced the question "will he be a good servant of the hospital?"—meaning would he be able to observe and deal with the whole of the sick man. Dr. Davidson hoped that the Royal Colleges and the senior members of teaching hospitals would exert their influence to obtain for the student a broader education.

The PRESIDENT observed that the remedy for some of the defects exposed in the discussion lay in proper recognition of the general physician and the general practitioner. Certainly it was for the general practitioner to decide when, and from whom, specialist advice should be obtained. Present evils had many roots, one of which was the examination system.

Reviews of Books

Bacterial and Virus Diseases

Antisera, Toxoids, Vaccines, and Tuberculins in Prophylaxis and Treatment. H. J. PARISH, M.D., clinical research director, Wellcome Foundation. Edinburgh: E. & S. Livingstone. 1948. Pp. 168. 7*s.* 6*d.*

KNOWLEDGE of immunological principles and the proper application of that knowledge is often found wanting among practitioners of medicine, perhaps because this branch of pathology is badly taught or difficult to comprehend. In this small volume, both student and practitioner—and it is for them that the book is primarily written—will find the theory and practice of immunology set out in simple language and with just enough detail to guide the doctor when seeking advice on how and when to protect a child against measles, diphtheria, or a variety of other bacterial and virus infections. Although today serotherapy has been largely replaced by chemotherapy, chapters are devoted to the use of antitoxins and antibacterial sera for both prophylaxis and treatment of the appropriate infections. There is advice about tuberculin-testing and the use of B.C.G. vaccine, a timely discussion of the techniques and readings of anti-smallpox vaccination, which nowadays will more often fall to the lot of the private practitioner, and simple instructions about the use and sterilisation of syringes (but the appropriate size of needle for different injections is not mentioned). No doubt the teacher and public-health worker would have welcomed a fuller discussion on the pros and cons of the more debatable practices, but a book of this small compass is obviously meant to be a vade-mecum for the practitioner rather than a reference book for the expert. As such it will meet a real need, particularly if the general practitioner plays his part in preventive as well as in curative medicine.

Cytologie sanguine, normale et pathologique

M. BESSIS, directeur du laboratoire de recherches du Centre National de Transfusion Sanguine. Paris: Masson 1948. Pp. 298. Fr. 1500.

THIS interesting product of the French school of hæmatology is well worth looking at. Most of the contents will be familiar to any English reader, and the techniques and nomenclature now used in France are evidently very similar to those used here. The 19 colour plates are well done in a somewhat diagrammatic manner that shows a clearer picture of nuclei and cytoplasmic detail, and purer, more contrasted colours, then one actually sees down the microscope. There are many photomicrographs, some of which are first-class.

The interesting parts of this book are the sections that are unfamiliar. Bessis does not limit himself to blood and bone-marrow; many of the cells he pictures are obtained from lymph-gland puncture—a technique he uses extensively. It is material from lymph-glands that enables him to illustrate the appearance in smear preparations of histioblasts, histiocytes, "mastocytes," and the "eosinocytes" that are prominent in Hodgkin's disease. A striking series of 4 colour plates illustrate the evolution of Sternberg-Reed giant-cells from reticular macrophages.

Bessis diverges notably from Anglo-American practice in his description of the most primitive forms. He distinguishes a "hæmohistioblast" resembling a reticulum cell that gives rise to: (1) a hæmocytoblast from which derive all blood cells except the monocyte, and (2) a histioblast from which all free tissue cells and blood monocytes derive. Plasma cells develop from the histioblast. Like many Continental writers, he describes paramyeloblasts and a paramyeloblastic leukæmia; he goes further and distinguishes parahæmocytoblasts and paramonoblasts—and here it is difficult to follow him. Classification of the red-cell series is on familiar lines; he believes in "intermediate" forms between normoblasts and megaloblasts, but he admits that "certains Anglo-Saxons" are not convinced about this.

Despite the very detailed morphology, Bessis does not lose sight of the general picture, and in a typically French passage he puts succinctly a principle that many have emphasised: "comme toujours en cytologie morphologique, c'est le contexte qui compte." In an equally French manner, the literature is almost entirely confined to the French. The book is printed on excellent paper, but wretchedly bound in paper covers.

Religion and Psychotherapy

A. GRAHAM IKIN, M.A., M.SC., PS.F., national president, British Federation of Psychologists, 1948–49. Birmingham: Rylee. 1948. Pp. 112. 5*s.* 6*d.*

THIS is an age of specialism in which one kind of expert is prone to dismiss the ideas of another kind of expert as fantasy. The author of this book is well equipped for her attempt to further a rapprochement between psychotherapy and religion. She wants the medical profession and the clergy to act as allies and not as enemies, and she believes this will happen only when psychologists recognise that religion is an integral part of human experience and when the clergy are able to speak in the name of religion rather than of particular sects or denominations. Both professions at present suffer from holding limited views. "The medical man who limits insight and knowledge to his own profession falls into the same mistake he so condemns in the clergyman's attitude towards some denominational church. Exclusiveness is the expression of narrowness, not of wisdom."

The Hormones

Physiology, Chemistry and Applications. Vol. I. Editors: GREGORY PINCUS, KENNETH V. THIMANN. New York: Academic Press. 1948. Pp. 886. $13.50.

THIS is the first of two volumes in which an effort will be made to give "a comprehensive presentation, at the research level," of all our knowledge of hormones. The list of contributors is a guarantee that the treatment will be authoritative and thorough.

About a quarter of this volume is devoted to plant hormones, and hormones in insects and crustaceans: the chapter on insect hormones contains a short but fascinating discussion of the "gene hormones," a subject where chemistry and genetics meet. The remainder is concerned with mammalian hormones; the material dealt with "is largely a matter of convenience rather than principle" and perhaps a more rational division might have been worth attempting. The

Digitized by Google

main emphasis is on the chemistry and metabolism of steroid hormones—i.e. œstrogens, progesterone, androgens, and adrenal cortical hormones—but there are also chapters on the chemistry of anterior-pituitary hormones, on the hormonal control of mammary growth and of lactation, on the hormones of the gastro-intestinal tract, on the physiology and chemistry of the parathyroid hormone, and on the internal secretions of the pancreas. The discussion by Pearlman of the chemistry and metabolism of the œstrogens deals fully with the natural œstrogens and with the doisynolic acid types of compounds; presumably the chemistry of the synthetic œstrogens will be considered in the second volume.

The book is packed with information: there are well over 3000 references, and the reader can expect to find, a wide and informative discussion on any topic included, though there are very few illustrations. It will be valuable to those engaged in hormone research and those seriously engaged in teaching the subject.

Introduction to Clinical Orbitonometry

A. C. COPPER, M.D., ophthalmological department, University of London. Leiden: H. E. Stenfert Kroese. London: H. K. Lewis. 1948. Pp. 125. 11s. 6d.

SINCE von Graefe drew attention, in 1886, to the fact that there is a variable degree of resistance when pressure is applied to the eye, backwards into the orbit, many attempts have been made to evolve apparatus that would measure this resistance. But none of these attempts have led to clinically satisfactory methods, and the procedure evolved by Dr. Copper holds more promise. He measures the backward displacement produced by known (variable) pressures applied with a dynamometer, and he gives his findings in normal persons and in conditions such as thyrotoxicosis (treated and untreated), acromegaly, and retro-ocular swelling. He holds that with inflammatory infections of the nasal sinuses intra-orbital involvement can be recognised by his method at a very early stage.

The Digestive Tract in Roentgenology

JACOB BUCKSTEIN, M.D., visiting roentgenologist, Bellevue Hospital, New York. Philadelphia and London: J. B. Lippincott. 1948. Pp. 889. 100s.

FOR more than 25 years Dr. Buckstein has been correlating radiological with operative and post-mortem findings in diseases of the gastro-intestinal tract. This monumental volume is the result not only of vast experience but of a wide search and discreet use of the literature. The common disorders which are the everyday work of an X-ray department are fully defined. Every rare abnormality or disease is also included, but the stress is always on the common and not on the rare conditions. The style is clear, and even the illustrative case-histories are easy to read. There are over 1000 illustrations. Dr. Buckstein rather timidly suggests in his preface that the volume might be of interest to the general practitioner. It is much too specialised for practitioners, but it should certainly occupy a prominent place in every X-ray department.

Modern Trends in Diagnostic Radiology

Editor: J. W. MCLAREN, M.A., M.R.C.S., D.M.R.E., director, X-ray (diagnostic) department, St. Thomas's Hospital, London. London: Butterworth. 1948. Pp. 464. 60s.

THIS volume contains 31 articles by various authors. A few are no more than brief résumés of current thought and procedure: but the majority will be of considerable value both to radiologists and clinicians. There is no attempt to cover the whole field of radiology, and the selection is rather patchy: gastro-intestinal conditions deserve at least as much space as the lungs. Though it may be invidious to select a few articles from so many that are worthy of study, special mention must be made of three: Baclesse on tumours of the pharynx and larynx, Meiklejohn on pneumonoconiosis, and Barnard on tumours of bone are outstanding. It is difficult for the editor of a collection of invited articles to do much editing, but Dr. McLaren might have allowed fewer liberties with the King's English on the part of foreign authors. The illustrations are generally good; the printing is excellent, but the binding is poor.

The Year Book of General Surgery, and the Year Book of Urology, for 1948 (Chicago: Yearbook Publishers. London: H. K. Lewis. Pp. 717 and 445. 25s. and 26s.).—These two volumes in the well-known series are now available, and as usual carry a thought-provoking quiz on the dust jacket, and a capable survey of the year's work inside. "General Surgery" is edited by Dr. Evarts A. Graham, and "Urology" by Dr. Oswald S. Lowsley.

British Encyclopædia of Medical Practice: *Medical Progress and Cumulative Supplement, 1949.* (London: Butterworth. Pp. 409 and 423. 50s).—This year Lord Horder once more leads his strong team on to the field with confidence. In his foreword he particularly recommends to readers the discussions on hypertension and cardiovascular surgery as illustrating the coöperation of the physician and surgeon, and he also notes the gradual shift of attack of poliomyelitis from children to adults. An instructive commentary on the *British Pharmacopœia 1948* has been included, and the section on drugs contains a useful list of new preparations. The classified abstracts which complete the volume cover medicine from Abdominal Pain to Whooping-cough, and the cumulative supplement brings the encyclopædia up to date by adding knowledge and opinion accepted since its publication.

Clinical Chemistry in Practical Medicine (3rd ed. Edinburgh: E. & S. Livingstone. 1949. Pp. 324. 17s. 6d.).—C. P. Stewart and D. M. Dunlop provide one of the few English textbooks covering the field of clinical biochemistry well, and their book is in many ways more practical and readable than similar American works. There are some fourteen chapters describing investigations on basal, carbohydrate, mineral, and water metabolism, and the various tests of renal, gastric, pancreatic, and liver function. A useful introductory chapter deals with material for analysis, interpretation of results, and the significance of normal values. Details of the more important biochemical methods of analysis are given in an appendix. The book contains no references, and in some cases the authors' choice of methods is open to argument; but they point out the limitations, as well as the values, of the various tests described.

On Life and Sex (London: Heinemann. 1948. Pp. 282. 7s. 6d.).—In his lifetime Havelock Ellis earned our gratitude. Seeking to increase the freedom and scope of thought, he battered at some of those taboos which, past their usefulness, remained only to impede. His especial province was the study of sex: with Freud and others he helped to introduce us to the facts of our existence. Two acts were needed—presentation of the facts, and their tentative assessment. Freud was devastating in the first; Havelock Ellis attempted the second. These two series of essays were first published in 1920, and again in 1935. They are now republished conveniently in one volume. Time has made them a little commonplace, as the author in his preface to the second series feared it might; for though they are sound and sane they occasionally seem unnecessarily impassioned. But the second series have a mellowness and breadth of outlook which make for easy reading; and they still have their lessons to teach.

Textbook of Medical Treatment (5th ed. Edinburgh: E. & S. Livingstone. 1949. Pp. 999. 35s.).—This textbook, edited by Prof. D. M. Dunlop, Prof. L. S. P. Davidson, and Prof. J. W. McNee, gives the practitioner just the practical guidance that he wants in his everyday work. Clear without being dogmatic, it covers the whole field of general medicine in an orderly way. The authors have all aimed at giving lucid instructions, and where possible the principles on which treatment is based. Generally a short introduction, with a brief account of ætiology and prevention, precedes detailed schemes of treatment—in which, moreover, relief of symptoms is not ignored. It is particularly helpful to find the pharmacological instructions and toxic effects of drugs so fully given. Some of the condemnatory opinions on doubtful or uncertain forms of therapy are refreshingly frank, and readers will be grateful for not having too many alternative treatments offered them without sufficient emphasis upon any one. The fifth edition includes fresh work on the anti-histamine drugs, dehydration, and penicillin. The names of four new contributors appear in this edition, and the useful list of proprietary preparations, with their official equivalents, has been revised by Mr. Mair.

Digitized by Google

THE LANCET

LONDON: SATURDAY, APRIL 2, 1949

The General Practitioner

EVERYONE agrees that more doctors are required; the Socialist Medical Association [1] estimates, indeed, that the aggregate of practising doctors in Britain ought to be raised by some 15,000, bringing the total to 54,000, of whom 27,000 would be in general practice. To train the extra numbers the association calls for "six or eight additional schools founded in association with the newer universities and what were till July 5 last the larger municipal hospitals." Unless the content of the curriculum were altered, the creation of these new schools would have no early effect; for the shortage of laboratory space and skilled preclinical teachers which now besets our established schools would probably be even greater at new centres: moreover, under the most favourable conditions it takes a long time to gather a suitable teaching staff, and even longer to weld them into a team. It can be argued, however, that the need is so urgent that the number of students should be extended even if this means less comprehensive training, and in our present issue Dr. PLESCH says that the public would in fact be better served if we turned out twice as many general practitioners of a lower academic grade. For general practice, he believes, a four-year vocational course would suffice; and the more academic training provided by the present teaching hospitals should be reserved for the future consultant, specialist, and scientist. Retrograde as this proposal may seem, it is none the less in line with the present tendency of the overburdened general practitioner to disuse his medical skills and practise medicine on a level little above that of a competent orderly. If we are going to be content with conditions under which real medicine is to be practised almost exclusively at or from hospitals, why not frankly acknowledge the fact and accept Dr. PLESCH's proposal to train our students accordingly?

But are we content? Do we think that the public would do better if the emphasis shifted further towards the hospital, and if general practice were undertaken by a lower grade of practitioner whose chief function would be to refer everything difficult to a specialist? The fate of the really ill patient would still depend often on the speed with which his family doctor recognised the disorder and referred him to hospital; delay of a few months with early tuberculosis, and of a few hours with perforated peptic ulcer, can make the difference between life and death. The practitioner might be said to have done his job if he perceived that hospital treatment was needed, and how soon. But even this calls for clinical skill; and experience already shows that, denied clinical responsibility, the practitioner will not develop and maintain that skill. If, then, the hospitals are to take over the treatment of more of the serious illness, they must expect that more patients will reach them late, and thus that more will stay longer and more will die. Already the hard-pressed practitioner sends to hospital many of the cases he would formerly have treated; but in quickly detecting, amid the hubbub of the present-day surgery, which of his patients need expert attention, he is able at least to call on a fund of clinical knowledge gathered in the more leisurely days before July 5. The young man entering practice has no such fund, and now has less chance of accumulating it; so for him the formal training at the university and in the hospital is more than ever important.

That most of the patients with major disorders should be seen at hospital appears at first sight a neat arrangement. But will the patient accept the discomfort of more frequent visits to outpatient departments, and will he in the end be better served? As things stand, he is increasingly likely to find himself in the care of one or more special departments, with nobody to coördinate his investigation and treatment; and too often he will be offered the knowledge of specialists rather than the wisdom of a consultant. In the Royal Society of Medicine's discussion last week on specialisation,[2] all the leading speakers deplored the passing of the general physician and the general surgeon; and the scarcity of such men makes it more than ever necessary that the practitioner should keep his position as the patient's ultimate adviser. Sir HENRY COHEN was right in implying that the practitioner, while drawing freely on specialist advice, should retain control of his patient; and that in hospital all patients should go first to the consultant, who might then refer them to his specialist colleagues. In this light both the consultant and the practitioner are seen as coördinators; each, in his own sphere, has an interest in the whole man.

> "The most important thing about any ailment," said a correspondent recently,[3] "is the patient's attitude towards it, and the extent to which the ailment is allowed to interfere with the patient's normal life and activities. A diabetic who lives for his diabetes, however correctly and successfully, leads a worthless life compared with the patient who ignores it and goes about his business unconcernedly. It is the duty of the general practitioner to cultivate this unconcern, having previously reached his own conclusion about the extent to which the disease may be allowed to dominate the patient in any given case. . . . It is perhaps this function more than any other which constitutes the specialty of the general practitioner; certainly no-one within the profession claims to compete with him or lays claim to the experience which is needed to guide the patient through a maze of difficulties to the right decision about himself."

But if the practitioner is to play this important part he must remain a doctor and not be reduced to an orderly or a clerk. He must receive a broad basic training; he must have ready access to the means of diagnosis, as well as contact with the hospital consultant and specialist; he must have opportunity and time, through the provision of health centres and through increased recruitment, to apply his mind to clinical problems; and he must have suitable pay and prestige, if only to ensure that he is joined by able colleagues. Today not one of these conditions is satisfied; and those who see that sound general practice is vital to the health of the National Health Service, and to the proper care of the public, view the future with more and more foreboding.

1. Memo. E53/48. Published by the Socialist Medical Association, 86, Rochester Row, London, S.W.1.

2. See p. 568.

3. *Lancet*, March 12, p. 454.

Digitized by Google

Surgery of Mitral Stenosis

IN 1902 Sir LAUDER BRUNTON [1] contributed to these columns a preliminary note on the surgical treatment of mitral stenosis, and later that year he described an operation for this disorder.[2] It must then have seemed that a new era was dawning in the therapy of rheumatic heart disease; but many years passed before any real advance was made.

Early in the '20s ELLIOTT CUTLER,[3] in Boston, carried out a series of operations, first in animals and later in man, designed to excise partly the cusps of the stenosed mitral valve. For this purpose he had devised a valvulotome, which was introduced through the wall of the ventricle after incision of the pericardium and dislocation of the heart. In 1923 he was able to report recovery of a patient after such an operation,[4] but his subsequent experiences were disappointing. Only one other contribution at that time need be mentioned: this was SOUTTAR'S [5] successful digital dilatation of a stenotic mitral opening. The late war provided many instances of foreign bodies lodged in the heart and great vessels; and the surgical treatment of these made for better understanding of the general principles of intracardiac surgery. DWIGHT HARKEN and his associates [6] found that dislocating the heart to make it more accessible, seriously impaired its action; when left in its natural position the heart withstood far more severe operative manœuvres. HARKEN and his co-workers think that the mitral valve should be approached through the left auricle or a branch of the pulmonary vein; in this way the mitral opening is more easily engaged than with CUTLER'S approach through the left ventricle, for the valvulotome is guided towards the opening as if into a funnel. HARKEN'S valvulotome—basically the same as CUTLER'S—is curved, and the trocar and cannula close to form a blunt instrument. When inserted into the mitral orifice the cutting blade can be exposed on either side, and the portion of valve resected is retained by the instrument. HARKEN tries to enlarge the stenotic orifice in such a way as to produce minimal regurgitation of blood and maximal restoration of valvular function; approaching through the auricular appendage, he cuts the posterior valve centrally and then laterally, to remove the rigid commissural bridges.[7] Thus HARKEN'S technique differs from CUTLER'S in that the heart is not disturbed from its normal position, the mitral valve is approached from the auricular side, and the posterior leaf of the valve is cut in preference to the anterior. In comparing results with the two procedures, it has to be remembered that methods of replacing blood lost at operation have been greatly improved since CUTLER'S reports appeared.

For the purpose of operation HARKEN and his team classify patients with mitral stenosis into three main groups, with a different procedure for each. The first group is made up of patients with a low resting cardiac output which does not rise on exercise and may even fall; the pulmonary arterial pressure is high, and right-ventricle failure is usual. Such patients are submitted to the valvuloplasty already described. The second group comprises those with a cardiac output which, though normal at rest, rises on exertion; typically they have a high pulmonary arterial pressure with severe lung symptoms, and the regurgitation is probably more important than the actual stenosis. Here treatment consists in making an interatrial defect, which results in a Lutembacher's syndrome, with pressure shunted from the left to the right side of the heart, after the manner of a safety-valve. This is a formidable undertaking; and SWEET and BLAND [8] have achieved a similar shunt outside the heart by anastomising the azygos and pulmonary vein. HARKEN believes that the ideal treatment for mitral stenosis would be the introduction of polyvinylethylene valves; these have already been tried with success in dogs. The third group of patients are those completely disabled by mitral disease; on the least exertion they develop tachycardia, often accompanied by severe pain which is not controlled by medical measures. For them HARKEN performs bilateral sympathectomy of the cardiac accelerator nerves—an operation similar to that successfully employed by WHITE and BLAND [9] for the relief of severe angina pectoris.

1. Brunton, L. *Lancet*, 1902, i, 352.
2. Brunton, L. *Ibid*, p. 547.
3. Cutler, E. C., Levine, S. A. *Boston med. surg. J.* 1923, 188, 1023.
4. Cutler, E. C. *Arch. Surg.* 1926, 12, 212.
5. Souttar, H. S. *Brit. med. J.* 1925, ii, 603.
6. Harken, D. E. *Surg. Gynec. Obstet.* 1946, 83, 117. Harken, D. E., Williams, A. C. *Amer. J. Surg.* 1946, 72, 80. Harken, D. E., Zoll, P. M. *Amer. Heart. J.* 1946, 32, 1.
7. Harken, D. E. Lecture at Boston City Hospital, Jan. 11.
8. Bland, E. F., Kelley, R. M., et al. *Amer. Practit.* 1948, 2, 756.
9. White, J. C., Bland, E. F. *Medicine, Baltimore*, 1948, 27, 1.
10. Denny-Brown, D. Disease of the Basal Ganglia and Sub-thalamic Nuclei. New York, 1946.
11. Hall Sir A. *Lancet*, 1943, i, 193.

Management of Parkinsonism

THE daily press these days is giving increasing publicity to medical news, and announcements of discoveries or advances naturally receive particular attention. This is inevitable, being a reflection of public taste and a tribute to the rapidity of medical progress; but the trend has several disadvantages. Modest claims may be unintentionally exaggerated and distorted, so that needless distress is inflicted on the sick by raising their hopes prematurely. Again, patients who read the newspaper accounts may lose confidence in their doctors who show a healthy caution in applying new remedies; and of late there have been several misguided attempts on the part of the public to force research along specific lines, regardless of the fact that valuable advances are rarely so made. The parkinsonian states have not escaped the spotlight, and an impression seems to be growing that the new drugs have overcome all the outstanding difficulties.

The general management of these cases is probably still as important as the particular drugs used. DENNY-BROWN [10] reminds us that the patient expends much more energy than the normal person on the simplest of actions; for him true rest is impossible save in sleep. His strength must be husbanded for essential purposes, and though regular exercise is necessary it should be distributed over all joints and not confined to walking. Light massage may be beneficial, but deep massage or electrical treatment is contra-indicated. According to HALL [11] a suitable spinal brace is occasionally of value to those whose posture encourages festination, and he also noted that such people often find riding a bicycle easier than walking. One of his patients preferred to take his meals at night, when rigidity tends to be less severe. The patient should be helped to adopt a healthy

Digitized by Google

mental attitude to his disorder, and encouraged to continue in some form of employment for as long as possible. His ability to cope with his symptoms is largely determined by psychological factors, and the superimposed affective disorders can often be overcome by attention to the details of his general life. Whether these patients should be encouraged to mix with one another is questionable; in what is typically a slowly progressive disorder the disadvantages of such society may heavily outweigh its benefits.

The action of hyoscine in lessening parkinsonian rigidity, first noticed, it is said, by GNAUCK in 1882, is shared by all the solanaceous drugs. Unfortunately their mode of action is as yet unknown. Preparations of hyoscine or stramonium are usually preferred to atropine or hyoscyamus because the latter have a longer-lasting effect on accommodation. Special preparations made from Bulgarian belladonna seem to have been convincingly shown to possess no advantages over active pharmacopœial preparations.[12] Patients with paralysis agitans, being older, tolerate such drugs much less readily than postencephalitics, in many of whom the dosage can with advantage be pushed far beyond pharmacopœial limits. Paresis of accommodation (causing dimness of vision) and dryness of the mouth can be reduced with eserine eye-drops, special lenses, and the addition of pilocarpine nitrate; but dizziness, headache, mental confusion, diarrhœa, and urinary retention are toxic symptoms which indicate that the limits of tolerance have been passed. Amphetamine in suitable dosage will sometimes diminish rigidity, check oculogyric crises, and improve the mental state, though its effects are rarely striking. It is more important to ensure sufficient sleep, and for this barbiturates are often called for. In the last two years much has been heard of an entirely new compound, 'Parpanit,' a substance closely related to antispasmodics such as 'Transentin' and 'Dolantin'; it has an atropine-like action, though we do not know how it works in parkinsonism. DUNHAM and EDWARDS,[13] after a careful assessment of its value, concluded that its activity and side-effects are somewhat similar to those of the solanaceous drugs. The new preparation may help when older remedies are not well tolerated, but in most cases nothing would be gained by abandoning the solanaceous drugs. More recently RYAN and SPURWAY WOOD [14] have reported favourably on 'Benadryl' in parkinsonism. They treated some 40 cases with 50 mg. three to four times daily, and none showed any toxic effects apart from sleepiness in the first fortnight, though 2 patients had taken such doses for over eighteen months. Rigidity was consistently improved and muscular cramps rapidly abolished, though tremor and oculogyric crises responded poorly. They remark that benadryl, though effective when given alone, can be used in conjunction with solanaceous preparations. A correspondent last week reported less happy experience; but it seems at least that the anti-histamine drugs deserve an extensive trial in this disease.

Surgical relief of tremor, which often does not respond well to medical measures, has been considered. The various procedures have been discussed by BUCY,[15] KLEMME,[16] and others. In brief BUCY recommended extirpation of the precentral cortex, including both areas 4 and 6 of Brodmann, though he was reluctant to attack the "arm area" of the dominant cortex, because a complete though temporary expressive aphasia resulted. MEYERS [17] found removal of the head of the caudate nucleus beneficial, and section of the lateral pyramidal tract in the cervical cord, as described by PUTNAM,[18] reduced tremor considerably without producing much weakness in the limbs. This last procedure has the advantage of avoiding cortical extirpation with all its attendant risks. But seven years have elapsed since this report was published, and it seems that most neurosurgeons on both sides of the Atlantic do not regard the procedures with much enthusiasm. None of them is entirely satisfactory, and since in general they are only suitable for young patients with a disabling tremor largely confined to one side, it is fair to say that surgery still cannot benefit most cases.

It is too early to claim that great advances in the treatment of parkinsonism are being made. We are still ignorant of how the older remedies act, and we may not get much further until we learn more about the disorders of function which characterise these complaints. The author of the Disabilities article of Feb. 26 remarked that the ease with which tremor can be turned on and off by a dose of a solanaceous mixture provides an opportunity for studying the mechanism of tremor. It rests with us to make the position clear to patients with parkinsonism, so as to save them needless disappointment; but a great deal can be done for them by studying the details of their management.

1899–1949

IN its fifty years of life the School of Tropical Medicine opened by MANSON in 1899 has gained world-wide renown; and the annual report for 1948 of this school and of the London School of Hygiene, with which it is now conjoined, says that of 289 students who have completed courses in tropical medicine since the late war, 157 came from twenty-nine countries outside Britain. Of recent years the schools of tropical medicine have been joined in their endeavours by powerful groups such as the World Health Organisation; but in welcoming this access of strength Prof. GEORGE MACDONALD warns us that the school, to sustain its reputation for independent work, must continue to cultivate its own field. Prof. J. M. MACKINTOSH, the dean, points to the need for still greater effort in the prevention of disease and the promotion of health in the tropics. There is, he says, room for fresh scrutiny of the school's work, since the peoples of tropical lands stand on the threshold of an "era of cultural and material development in which their own sons and daughters will play a leading part." This point is taken up by Prof. B. S. PLATT, who observes:

> "Whilst members of societies as highly developed as our own have derived immense benefits from the results of the work of scientists, the majority of the peoples of the world, particularly those in tropical countries . . . have for the most part benefited to only a small extent; indeed the results of 'progress' have sometimes been detrimental to their health and well-being."

The rest of the report shows that this rueful thought is also in the minds of others who are planning for the next fifty years.

12. Alcock, N. S., Carmichael, E. A. *Quart. J. Med.* 1938, **7**, 565. Hill, D. *Lancet*, 1938, ii. 1048.
13. Dunham, W. F., Edwards, C. H. *Lancet*, 1948, ii, 724.
14. Ryan, G. M. S., Spurway Wood, J. *Ibid*, Feb. 12, p. 258.
15. Bucy, P. C. *Res. publ. Ass. nerv. ment. Dis.* 1942, **21**, 551.
16. Klemme, R. M. *Ibid*, p. 596.
17. Meyers, R. *Ibid*, p. 602.
18. Putnam, T. J. *Ibid*, p. 666.

Digitized by Google

Annotations

LONG-TERM ANTICOAGULANT THERAPY

THE value of dicoumarol in the treatment of acute cardiac, venous, and arterial thrombotic states, has been established. Now it is suggested that the drug may be given, over months and even years, as a preventive in conditions where clots continue to form. With such prolonged treatment estimation of blood-prothrombin at the customary 2-day intervals is not feasible; but Foley and Wright [1] suggest that after 3 weeks' observation with frequent estimations, the daily dose of dicoumarol needed to keep the prothrombin at the therapeutic level—which means a prothrombin-time about twice the normal—will be known. They believe that under stable conditions the maintenance dose varies little, and that the interval between estimations may be extended to $3^1/_2$ days, and later to a week or even longer if the values are keeping fairly steady. In nineteen cases the average dose of dicoumarol per week varied from 300 to 800 mg. An increased dicoumarol effect after taking alcohol was noted; this is probably due to mild liver toxæmia, for a similar increase has been observed in cardiac failure with congestion of the liver.[2] A change in dosage was also sometimes necessary at the time of menstruation; most patients then needed less, but one required more. Clearly the patient must be reliable and intelligent—one who will exactly follow the instructions and report any intercurrent event. Of the nineteen cases reported by Foley and Wright, four had mitral stenosis, three phlebitis migrans, seven recurrent phlebitis, and five cardiac infarction. They were given dicoumarol for periods of 5–20 months without any serious hæmorrhages (despite prothrombin-times which sometimes rose inadvertently to 300 seconds), and without detectable damage to liver or kidneys. Each of these patients had previously suffered from thrombo-embolism, but none had a further attack while the prothrombin was maintained at a therapeutic level. For carefully selected patients this new procedure seems to be justified.

PHARMACOLOGICAL AIDS IN PSYCHIATRY

Prof. Jean Delay recently visited London to discuss the preliminaries of the International Congress of Psychiatry, to be held under his presidency in Paris in 1950. During his stay Professor Delay addressed the section of psychiatry of the Royal Society of Medicine on the use of drugs in exploring the personality of neurotic subjects and in their treatment. He briefly reviewed the field since Moreau de Louis published his paper on hashish in 1845. Professor Delay's own studies have been chiefly concerned with the barbiturates and with amphetamine and its derivatives. He has found that the barbiturates, which are widely used in "narco-analysis," have the effect of lowering intrapsychic tension and depressing psychological tonus. 'Methedrine,' in contrast to this, increases intrapsychic tension and acts as a stimulant; intravenous injection of 30 mg. produces severe changes, with considerable rise in blood-pressure and emotional stimulation. Its effect varies in different mental disorders. Thus in manic illness it produces a violent outburst of excitement, while in depressive states it increases the agitation and misery. If the depressed patient is stuporose, it increases the pressure of anxiety and so makes it possible for him to talk about his feelings and beliefs. Schizophrenic patients respond to methedrine with intensification of any catatonic features they may show; their efficiency in performing intellectual tests is impaired by the drug, but on the Rorschach test their responses become more numerous and prompt. For acute neurotic disorder methedrine helps towards emotional abreaction, and favours the expression of thoughts consciously known to the patient but partially suppressed. Some therapeutic benefit can be obtained by repeated administration of the drug to patients with chronic neurotic illness, though the benefits here are more doubtful; however, the psychasthenic conditions, in which 'Sodium Amytal' has failed, sometimes respond to methedrine. It also has limited use in the treatment of drug addiction, especially in relieving withdrawal symptoms. Professor Delay enlivened his polished address, which was delivered in French, with some vivid clinical narratives, illustrating the effect of narcotic drugs upon the processes of perception.

A survey of the work on methedrine done in Germany and the occupied countries during the war has been compiled by Edmund Tietze.[1]

TRAINING OF HEALTH VISITORS

Florence Nightingale first had the brilliant notion of sending nurses into the homes of the people to teach "household hygiene." In those days, as Dr. I. G. Davies and Dr. Fraser Brockington point out in a memorandum now being considered by the Society of Medical Officers of Health, infants died in slums and alleys to the tune of 150 in every 1000. Now, when the infantile mortality is down to 34 per 1000, there is a need to review the work of the health visitor and decide what duties she should cede to other social workers and what fresh work she should undertake. Davies and Brockington hold that antenatal care must now be left to the midwives and infant life protection has become the concern of the Home Office. But under the National Health Service Act local authorities are called on to employ medicosocial workers (who might well be health visitors) partly to help in the care and aftercare of sick people and by mental defectives, and partly to undertake preventive work. Another new duty laid on the authorities by the Act is visiting the home to give "advice"—doubtless general social advice and advice on hygiene—to all members of the family; and for this workers must have a thorough understanding of the social background. The hospital, too, needs to know the previous history and social background of patients admitted to the wards, and nowadays generally depends for it on the almoner. The writers of the memorandum believe that the hospital will be more fully informed if the health visitor becomes its link for this purpose with the general practitioner. They also note that the family is nowadays subjected to a constant stream of "visitors"—the health visitor, the school nurse, the almoner, the psychiatric social worker, the mental-health worker, mental-deficiency and venereal-disease social workers, the school-attendance and probation officers, and the officer of the N.S.P.C.C., the moral-welfare worker, the tuberculosis nurse, and the housing manager ("to mention," they say, "a few")—and that housewives would be glad to see some of these offices fused. At all events the health visitor's training might be reviewed with this in mind.

The report of the Working Party on Nursing, with its proposal for a two-year basic course, bears out their opinion that $3^1/_2$ years spent in hospital is too long a period for a girl training as a health visitor. Moreover, they feel that in comparison with the social-science worker, holding a university diploma, the health visitor is "tending to fall into the background." She is handicapped by lack of practical case-work; and her long stay in hospital makes it hard for her, they think, to get a wide grasp of the structure and economics of society. They therefore propose a new course of train-

1. Foley, W. I., Wright, I. S. *Amer. J. med. Sci.* 1949, **217**, 136.
2. See leading article, *Lancet*, Jan. 29, p. 189.

1. Experiences with Pervitin. Flat report P.B. 88826. No. 1206. Particulars from Board of Trade technical information and documents unit, 38, Cadogan Square, London, S.W.1.

Digitized by Google

ing for the health visitor, intended to make her eligible for most, if not all branches of social work." At present the shortest time in which a health visitor can qualify is 4 years; and she often takes 5 or 6. A university-trained social worker completes her course in 2 years, and is ready for work in her special field at the end of a further year's apprenticeship. The course proposed by Dr. Davies and Dr. Brockington would last $3^1/_2$–4 years, 2 years of which would be spent in a university and lead to a university qualification. During the first 18 months she would take the basic nursing training prescribed for all entrants to nursing by the Working Party; in the next 6 months she would take her "special" training at the university and in the public-health field, and at the end of it would sit the examination for State registration. The remainder of the training (18 months), to be spent in the university medico-social study course, would end in an examination for a diploma; but they foresee that this last period may need to be extended. They recommend that part I of the C.M.B. certificate should be dropped altogether from the health visitor's course. Obstetric work and teaching is properly done by midwives, and all the health visitor needs, they believe, is some knowledge of early signs of pregnancy, and of diseases of pregnancy and gynæcological disorders, and of the social implications of childbearing. Their proposed diploma course, which they see as a branch of the present diploma in social science, they give in some detail, and suggest that it would be appropriate also for almoners, industrial-health workers, and others. Besides the 6 months' "special field" study (which would include lectures on pædiatrics, elementary obstetrics, infectious diseases, dermatology, parasitology, hygiene of food, and occupational disease), the full diploma course would include the study of economics, medical and social history, social psychology, local and central government, social relations of disease, medicosocial problems of disease, environment and hygiene, social science and ethics, industrial relations, and medicosocial legislation and statistics. Case-work would be arranged on the same scale as for the present students taking the social-science diploma course.

UNDECYLENIC ACID IN PSORIASIS

A CHANCE observation has brought to light a new treatment for psoriasis. Impressed by a report [1] on the fungicidal and fungistatic action of fatty acids with low-boiling point on *Microsporon audouini*, Perlman [2] decided to administer such an acid by mouth to patients with tinea capitis; and for this purpose he selected undecylenic acid. The results were disappointing; but he observed that one effect of this treatment was profuse desquamation of the scalp, and he therefore thought that the drug might prove effective against psoriasis.

Perlman now reports 17 cases of chronic localised or generalised psoriasis where increasing doses of the acid have been administered by mouth for periods ranging from 8 to 191 days. In a few cases the lesions disappeared; in the remainder they were improved. Itching was completely relieved, and in several cases with troublesome arthropathy the joint pains disappeared. It seems that the acid promises the greatest benefit in subacute and chronic cases with generalised lesions. Exfoliation of the scalp begins very soon after treatment is started, and the lesions may start to retrogress within 2–3 weeks; affected nails are also improved. Perlman thinks that recurrence may be prevented, but as his experiments began only last April, this is not yet certain. He has also noted improvement in 8 cases of neurodermatitis treated in this way.

In psoriasis the best results were obtained with divided doses totalling 7·5–10 g. daily. Little is known about the toxicology of undecylenic acid, though tests in rabbits, mice, and guineapigs are said to have shown it to be relatively non-toxic. Some of Perlman's patients reported headache, nausea, vomiting, burning epigastric discomfort, or transient diarrhœa; several complained of an unpleasant taste in the mouth and of belching; and other manifestations included folliculitis, pustular lesions at the back of the neck, conjunctivitis, and axillary adenitis.

The path towards a cure for psoriasis is strewn with discarded remedies; but it is still too early to say whether or not undecylenic acid will add to the litter. Meanwhile, for severe cases the treatment of choice is still often the Goeckerman [3] régime, which involves the use of crude coal-tar, ultraviolet rays, suitable baths, and autohæmotherapy. In general practice this régime and its modifications have never achieved the popularity they deserve.

THE ESTIMATES

THE net cost of the National Health Service in Great Britain during the year 1949–50 has been estimated [4] at £259,727,600—an advance of £51,389,458 on the cost of £208,338,142 during the nine months' operation of the service in 1948–49. In the Civil Estimates,[5] now published, the gross cost of the service in the new financial year is given as £352,324,600, compared with £275,904,542 in 1948–49. The difference between gross and net costs is accounted for by appropriations in aid, which in 1949–50 are expected to total £92,597,000 (including £40,700,000 from the National Insurance Fund), as against £67,566,400 in 1948–49. The estimate of gross cost for England and Wales is divided as follows:

	1949–50	*1948–49*	*Increase*	*Decrease*
	£	£	£	£
Central Council &c.	16,000	10,000	6000	..
Hospital, specialist, and ancillary services	177,531,000	129,597,500	47,933,500	..
Services provided by local health authorities	14,025,000	9,283,000	4,742,000	..
General medical and dental services, pharmaceutical services, and supplementary ophthalmic services	102,392,600	80,321,500	22,071,100	..
Other services	18,705,000	28,384,542	..	9,679,542
	312,669,600	247,596,542		

For the general medical and dental, pharmaceutical, and supplementary ophthalmic services in England and Wales the estimates are as follows:

	1949–50	*1948–49*	*Increase*	*Decrease*
	£	£	£	£
Administration	2,029,000	1,606,000	423,000	..
General medical services	40,400,000	29,800,000	10,600,000	..
Pharmaceutical services	19,000,000	16,225,000	2,775,000	..
General dental services	28,204,000	19,000,000	9,204,000	..
Supplementary ophthalmic services	12,420,000	13,500,000	..	1,080,000

Advances to regional hospital boards in England and Wales are estimated at £147,180,000 for 1949–50, compared with £109,584,000 for 1948–49; and advances to boards of governors of teaching hospitals at £24,620,000, compared with £18,629,500. Under other services, transferred liabilities are expected to cost £1,858,000 in 1949–50, compared with £18,605,000 in the previous year.

1. Rothman, S., Smiljanic, A., Shapiro, A. L., Weitkamp, A. W. *J. Invest. Dermat.* 1947, 8, 81.
2. Perlman, H. H. *J. Amer. med. Ass.* 1949, 139, 444.
3. Goeckerman, W. H. *Northw. Med.* 1925, 24, 229; *Brit. J. phys. Med.* 1933, 7, 215.
4. 1949–50: Vote on Account. See *Lancet*, March 5, p. 404.
5. 1949–50: Civil Estimates for the Year ending March 31, 1950. Class 5: Health, Housing, Town Planning, Labour, National Insurance, and Contributions to Local Revenues. H.M. Stationery Office. Pp. 153. 2*s.* 6*d.*

Digitized by Google

THE PATTERN OF DISEASE IN INFANTS' HOSPITALS

IN his presidential address last week to the pædiatric section of the Royal Society of Medicine, Prof. J. M. Smellie analysed the relative incidence of the commoner diseases, and the relevant mortality, in 2306 infants under one year of age admitted between 1946 and 1948 to the infants' pavilion at the Birmingham Children's Hospital. The statistical value of such an analysis is limited; for, as Professor Smellie emphasised, the current policy of selection of cases for admission greatly influences the relative proportions. Among the many factors affecting such selection are the social conditions in the home, the suitability of the hospital, the availability of beds, the types of disease required for teaching purposes, the special interests of the pædiatrician concerned, and the preference of the pædiatrician for domiciliary or hospital care of children with various forms of illness. Mortality figures also are subject to a variety of modifying influences, notably the degree of illness regarded as warranting admission and the standard of hospital care; and these important factors are less uniform than methods of treatment.

It is instructive to compare the incidence of infective and non-infective diseases in the new and up-to-date centre at Birmingham with that in the older Edinburgh Children's Hospital, where, until the last few months of the period under review, infants were nursed with children of all ages in open wards. In the three-year period there were 904 cases of non-infective disease in Birmingham and 1274 in Edinburgh. In Birmingham the ratio of infective to non-infective cases is about 2 : 3, whereas in Edinburgh it is not fixed and in the period under discussion was almost exactly 1 : 1. The percentage incidence of the principal diseases in the two hospitals, by Smellie's classification, was as follows (Edinburgh figures in parentheses):

Infections.—Upper respiratory tract, 22·6 (4·3); bronchitis and pneumonia, 22·2 (31·5); gastro-enteritis, 19·5 (28·0); purulent meningitis, 5·4 (3·3); tuberculosis of all types, 3·0 (2·7); skin infections, 2·9 (3·5); other infections, 24·4 (26·7).

Non-infective Diseases.—Congenital abnormalities, 27·0 (20·6); pyloric stenosis, 23·5 (13·6); feeding disorders, 14·0 (16·8); hæmolytic disease of the newborn, 6·1 (2·4); prematurity, 5·7 (1·4); birth injuries, 2·9 (1·9); pink disease, 2·2 (0·5); intussusception, 2·1 (6·7); hæmorrhagic disease of the newborn, 2·1 (2·5); anæmia of later infancy, 1·7 (1·2); unclassified 12·3 (32·4).

Probably these figures are fairly representative of disease incidence in the types of hospital from which they come, subject of course to the selective influences already mentioned. In each type the broad outline is similar, respiratory and alimentary infection accounting for about two-thirds of the cases of infection. In the non-infective group congenital abnormalities, pyloric stenosis, and feeding disorders made the largest contributions, together accounting for two-thirds of the Birmingham and half of the Edinburgh admissions. More detailed analysis, however, reveals substantial difference in the proportion of cases of certain diseases admitted to the two hospitals. For instance, the upper respiratory tract was the site of 22·6% of the infections in Birmingham and only 4·3% of the infections in Edinburgh; this discrepancy is no doubt due to more stringent conditions for admission in Edinburgh and to differing interpretations of a vague diagnostic term. The much larger proportion of cases of pyloric stenosis, prematurity, and pink disease in the Birmingham series probably reflects greater willingness to admit infants with such diseases (in which infection is notoriously liable to occur when conditions are not optimal) rather than higher incidence.

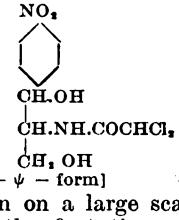
Mortality-rates correspond closely in the two series—but with a few notable exceptions. The Edinburgh figures were substantially higher for gastro-enteritis, pyloric stenosis, and feeding disorders, probably because the hospital could offer less modern facilities; and the inescapable conclusion is that in all large centres of population up-to-date units should be provided for infants. Without such units, the criteria of admission must be stringent; and many who would otherwise be treated in hospital are best kept at home.

SARCOIDOSIS OF THE NERVOUS SYSTEM

Colover [1] has lately described three cases, seen at the National Hospital for Nervous Diseases, where sarcoidosis involved the nervous system. One patient, a woman of 30, had bilateral uveoparotitis with peripheral neuritis and double facial paralysis; the condition subsided after a few months. A man of 56, who had had enlarged neck glands and some disturbance of taste for several months, developed polyneuritis with cranial-nerve palsies; but here, despite bilateral facial paralysis of lower motor-neurone type, there was no parotitis; lymph-node biopsy confirmed the diagnosis. The third patient, a woman of 23, after 2 years of headache and vomiting developed papillœdema and generalised ventricular dilatation; exploration of the posterior fossa revealed adhesive arachnoiditis obstructing the foramina of the fourth ventricle, and she recovered steadily after a new opening had been made to allow free circulation of cerebrospinal fluid. From a survey of 115 cases where sarcoidosis has been reported to involve the nervous system, Colover concludes that, though any part of this system may be affected, certain areas seem to be particularly vulnerable—the optic nerve and retina; the facial, glossopharyngeal, and vagus nerves; the pars intermedia of the pituitary; and the peripheral nerves. There may be meningoencephalitis or meningomyelitis, and localised sarcoid infiltration or tumour masses in the dura mater may develop; sometimes there is adhesive arachnoiditis, which may lead to hydrocephalus. The cerebrospinal fluid, if abnormal at all, exhibits a pleocytosis and increase of globulin. Thus this protean disease may produce disorders of the nervous system which, though the process is essentially benign and self-limiting, can easily be mistaken for more commonplace, and far graver, disturbances. Possibly the discovery of Wells and Wylie [2] that the gamma-globulin fraction of the serum-protein in patients with sarcoidosis sometimes contains a powerful tuberculin-neutralising factor may help in elucidating the essential nature of this mysterious condition.

SYNTHESIS OF CHLOROMYCETIN

THE Parke Davis Research Laboratories announce that a team headed by Dr. Leon A. Sweet, director of the research department of Parke, Davis & Co., has synthesised the antibiotic chloramphenicol ('Chloromycetin'). The formula is given as:



(*l*) — ψ — 1 para nitrophenyl-2-dichloro acetamido propane-l-3 diol.

[(*l*) — ψ — form]

Production on a large scale is being undertaken; and thus, for the first time, an antibiotic is being manufactured for use. Chloromycetin has given promising results in a number of infections, including scrub-typhus, typhoid fever, Rocky Mountain spotted fever, and undulant fever.

On March 25 the King knighted Prof. JAMES LEARMONTH and invested him with the insignia of a knight commander of the Royal Victorian Order.

1. Colover, J. *Brain*, 1948, **71**, 451.
2. Wells, A. Q., Wylie, J. A. H. *Lancet*, March 12, p. 439.

Digitized by Google

Special Articles

CONVALESCENT HOMES

THE NEED FOR MODERNISATION

SIR HENRY TIDY
K.B.E., F.R.C.P.
CHAIRMAN, CONVALESCENT HOMES COMMITTEE, KING EDWARD'S HOSPITAL FUND FOR LONDON

CONVALESCENT homes, as we now know them, first came into being about eighty years ago; but their use increased rapidly with the appointment of hospital almoners to attend to the interests of patients after discharge. Many of the oldest homes, which are still among the largest, were founded and staffed by religious communities. A few were established by special trades, such as printers. In recent years some of the larger hospitals have obtained homes—often by gift—confined to their own patients, a system which has both advantages and disadvantages. But a large number have been founded locally, some endowed by charitable individuals, others started by the energies of a committee which has raised the necessary funds in the surrounding district.

The favourite situation has been on the coast, in the East and South from Frinton to Bournemouth, and in the North on the coast of Lancashire. Consequently a great many homes were closed during the war, either by evacuation, enemy action, or requisition. The reopening of these involves many difficulties, not only of reconditioning, licences, and finances, but also of adaptation to the altered circumstances of today.

In 1946 King Edward's Hospital Fund for London undertook a preliminary survey of convalescent homes receiving patients from the London hospitals and the London area. The object was to find out generally whether help was needed after the war; but it soon became obvious that more extensive inquiries were necessary, and a committee for this purpose was set up by the council of the Fund in December, 1946.

The first necessity was to ascertain what convalescent homes existed or were planning to reopen. No comprehensive list had ever been compiled. Inquiries were made in various directions, especially from hospital almoners and from the Institute of Almoners, whose assistance has been invaluable. In April, 1947, the Fund was able to publish a directory containing particulars of about 100 homes in the Metropolitan areas, and in March, 1948, this list was enlarged to include nearly 150. Arrangements were then made for these to be visited.

DIVERSITY

The visitor to a number of homes is at once struck by the immense diversity in administration, size, type of patients admitted, and amenities. At one extreme are those equipped and staffed to deal with patients needing active medical and surgical treatment, some of these being little removed from what are often known as hospital annexes. At the other extreme are professed holiday homes, distinguished by accepting people who apply direct for accommodation—often referred to as "guests" rather than as "patients." The number of these latter is very small; but there are also a few, not greatly dissimilar, which require some form of recommendation from a doctor. These fulfil a useful function in providing rest and relaxation. Between these two extremes there is every gradation.

Diversity is evident in other things besides treatment. There is a wide difference between those which take adults and those which take only children. There is also great variation in size. Some successful homes have no more than 10 beds while the large institutions have room for over 200 patients. Certain homes for adults are restricted to limited sections of the population—e.g., printers, ex-Servicemen, "gentlewomen in reduced circumstances," civil servants, and nurses—but a large number are open to all. Children are divided by age and types of illness. Homes in which children stay for three months or more come within the scope of the Education Act, 1944.

This multiplicity may seem to be an anachronism in this age of large-scale planning, and some may think that a smaller number of large institutions would be more economical and efficient. But convalescence is a process in which the personal inclinations of the patient need to be considered if recovery is to be unimpeded. The essentials of convalescent treatment are fresh air, good food, and comfort, amid pleasant surroundings; and the definition of comfort and pleasant surroundings is a matter of taste. People who long for quiet and solitude have little in common with those who prefer to be surrounded by their fellow men and are able to enjoy games and recreations. Furthermore, when not feeling fit, many benefit from the atmosphere of a small establishment rather than that of a large one, however well run. Hospital almoners choose carefully the home they consider most suitable for each individual patient. Thus the argument for variety is strong and that for an economic unity is at its weakest in this branch of the health service.

THE NEW SITUATION

Under the National Health Service Act, 1946, institutions providing convalescent treatment were, like hospitals, transferred to the service. However, the Act, probably wisely, gave no definition of what constitutes convalescent treatment. As a result the Ministry of Health had to draw an arbitrary line between homes deemed to give convalescent treatment and those henceforth to be regarded officially as holiday homes. On the appointed day the former became part of the National Health Service, and in the Metropolitan regional areas these numbered about 57, with approximately 2900 beds.

Of the homes included in the Fund's directory, 83, containing 3856 beds, remain outside the service, and it is mainly with these that the Fund is now concerned. There may be a few more which the Fund has not as yet discovered. There are also an unknown number, probably as many again, elsewhere in England, of which no list exists, but which do not come within the Fund's scope.

Nearly all these homes, though outside the National Health Service, take some of their patients—and in many cases all—direct from hospital. Such patients are not well enough to return immediately to their own surroundings, or at least are in a condition to benefit from some further attention. Thus hospital beds are being released and a valuable function is being performed in restoring the health of the sick by means which cannot be available in hospitals. As a factor in the health service they are well worthy of consideration.

Many homes are small concerns, which were founded between the '80s and the first world war. Their endowments formerly enabled them to provide the means of recovery for poor people, either free or for a trivial charge. These endowments no longer suffice for this purpose, and in many cases are too small to maintain the buildings in a state of good repair, far less to modernise them. The National Health Service Act offers them great assistance, since its intention is to give all the sick a claim on the State funds, either through the hospital service or through the provision of part III of the Act, which lays the responsibility for preventive treatment and aftercare on the local health authority. In both cases a reasonable charge is recoverable from the authority responsible for sending the patients; so the anxieties of maintenance income should become less though by no means absent.

Digitized by Google

There remains, however, the difficulty of overtaking the arrears of repairs and modernisation which are now urgently required. The larger foundations, with very few exceptions, are faced with similar difficulties. The solution of this problem is the task which King Edward's Hospital Fund is now attempting, and its urgency is indicated by the present acute shortage of accommodation, especially during the summer months.

MODERNISATION

The Fund began by dealing with those out-of-date features which could be most rapidly rectified. The kitchen equipment was often sadly obsolete, and expert advice has been given on the redesigning of kitchens, and new equipment has been provided. Managing committees have willingly coöperated when their attention has been drawn to old-fashioned rules strictly governing the behaviour of the patients. Many surprising regulations have been cancelled, such as one forbidding male and female patients to speak to each other. The Fund has urged the abolition of "subscriber's letters" whereby subscribers could nominate patients for admission. The step calls to mind the early days of the Fund when voluntary hospitals were persuaded to abandon this system, which was then in general use.

These are small but important points. The Fund is now turning its attention to larger schemes of modernisation and is giving substantial grants towards capital expenditure.

A beautiful building in lovely grounds may still reveal a lack of imagination in the furnishings of the interior. Walls may be painted in depressing shades of dark green or dark brown, and prominently exhibit old prints of outmoded and uninspiring types. It is now becoming possible to obtain sufficient licences for redecoration to provide more cheerful surroundings.

The newer generation demands more facilities for washing and bathing than did its predecessors. This is usually an expensive item involving new building and extensive plumbing, and substantial contribution towards the cost has to be made by the King's Fund. Some homes doing good work are uneconomical because they are too small, and these are encouraged to make plans for extensions.

FRESH DEVELOPMENTS

There is, however, a further problem beyond the modernisation of existing homes. For some types of illness and disabilities there are not enough homes, or none at all. The Institute of Almoners in 1947 reported on this subject, but in the general state of hesitancy which preceded the appointed day nothing could be done. The unfortunate subjects of epilepsy are almost universally barred from existing homes, and the National Association for Mental Care, with the aid of a substantial grant from the Fund, has accordingly founded a small home, solely for epileptics. This has been so successful, and the applications for admission so numerous, that a second home is contemplated in which the Fund will be interested.

It is surprising that there is little accommodation for babies under two years of age. The Hampshire branch of the British Red Cross Society started a small home towards which the Fund gave help, and its success has led to the acquisition of a large house near Christchurch towards the purchase of which the Fund gave an initial grant of £5000. Homes are also scarce for adolescent boys, and for adults suffering from certain special conditions. These deficiencies cannot be rectified for some years, and large expenditure will be involved, but many schemes are under consideration.

Thus step by step knowledge has been acquired about convalescent homes, and this knowledge is being applied to good effect.

PALUDRINE IN MALARIA

DOSAGE FOR PREVENTION AND TREATMENT

THE following recommendations on the use of proguanil ('Paludrine') in prophylaxis and treatment of malaria, and suggestions for trial, are issued by the Colonial Office and the Medical Research Council on the advice of the Colonial Medical Research Committee. The recommendations are tentative and subject to review in the light of future experience and experiment.

PROPHYLACTIC USE

The dose recommended for suppression of malaria of all types, in endemic areas, is 100 mg. daily. For children the following dosage is advised: from birth to 5 years of age, 25 mg. daily; from 6 to 12 years of age, 50 mg. daily. When a daily dose is not practicable one dose of 300 mg. should be taken on the same day each week; dosage for children should be in the above proportion. In the case of persons (other than indigenous inhabitants) who have been resident in an endemic area for some time, or who have been otherwise already exposed to malarial infection, a full therapeutic course (see 1[*a*] below) should be taken before entering on the suppressive regimen of paludrine.

THERAPEUTIC USE

1. *Plasmodium falciparum* (*malignant tertian*) *infections, mixed infections, undiagnosed type infections.*

(*a*) In the treatment of non-immunes, paludrine alone cannot always be relied upon to effect radical cure, and the clinical response with this drug unaided is also somewhat slow. It has been shown, however, that these disadvantages may be overcome by reinforcement with mepacrine on the first day of treatment. The following combined course is recommended for trial: 300 mg. paludrine twice daily for 10 days, reinforced on the first day of treatment with three doses of 300 mg. mepacrine, and followed by 100 mg. paludrine daily for six weeks. (Persons continuing to live in an endemic area should continue the suppressive regimen.)

(*b*) For treatment of the clinical attack in semi-immune subjects, such as labour forces and rural populations in endemic areas, a single dose of 300 mg. paludrine will usually suffice to produce clinical cure. Relapses can be treated similarly as and when they arise. Serious cases should be given emergent treatment (see below).

(*c*) For treatment of emergent conditions such as cerebral or algid malaria, and where for any other reason the patient is unable to take drugs by mouth, immediate intramuscular mepacrine or intravenous quinine therapy should be employed.

2. *P. vivax* (*benign tertian*) *infections.*

(*a*) Where the object is radical cure, the course advised for adults is 100 mg. paludrine plus 10 mg. pamaquin base (or a corresponding dose of one of the other 8-amino-quinoline derivatives) three times daily for 10 days; the dose for children should be proportionate. Pamaquin should not be given unless the patient can be kept in bed under medical supervision throughout the course; this is particularly important with children. When the patient cannot be kept in bed the alternative course recommended is 100 mg. paludrine three times daily for 10 days followed by a single dose of 300 mg. paludrine on the same day each week for a year.

(*b*) The treatment of the clinical attack in semi-immunes is as for M.T. malaria.

Unless otherwise stated, the dosage mentioned is that for adults. In recommending the use of a single dose of

Digitized by Google

300 mg. paludrine for the treatment of the febrile attack in semi-immunes and a weekly dose of 300 mg. for suppressive purposes, the advantages of these procedures are emphasised as (1) bringing an effective antimalarial drug within the economic capacity of village and rural populations of endemic areas of malaria, and (2) providing a method of prophylaxis easy of administration.

REMUNERATION IN HEALTH SERVICE

B.M.A. REPRESENTATIVE MEETING

A SPECIAL representative meeting of the British Medical Association was held last Tuesday under the chairmanship of Dr. E. A. GREGG, to consider the remuneration of general practitioners under the National Health Service Acts. The meeting had before it the report prepared by the General Medical Services Committee [1] which has been submitted to the Minister of Health. Dr. H. GUY DAIN explained that the committee was an autonomous body acting for general practitioners in the service, with power to go direct to the Minister. It was also a standing committee of the association, and though representatives could not alter what had been said to the Minister they were asked to show that the report had the weight of the association behind it.

Dr. S. WAND, chairman of the committee, in asking representatives for support, said that all over the country there was dissatisfaction about remuneration. Investigations in Lancashire, and later in other parts of the country, had shown that though on the whole the Spens recommendations, on the basis of a 20% betterment, were being implemented for the 40–49 age-group, there were too many low incomes in the under-40 group and too few larger incomes among the over-50 group. He thought the complaints were well founded, for the betterment bore an improper relationship to present-day money. There were also 2000–3000 more doctors in the service than had been expected, and the pool was therefore inadequate. But it would, he felt, be unreasonable to ask for 85% betterment when other sections of the community were not getting it. The report therefore recommended that the pool should be increased to bring in money for the extra doctors and to allow for a 70% betterment. It also recommended that the new moneys should be attached to the first 1000 patients on each doctor's list. He admitted that this was arguable, but it seemed at present to be the fairest method of helping the lower-income groups, and it would be reviewed later in the light of experience. The question of extra work undertaken by doctors under the service was being investigated.

HOW MANY PATIENTS ?

Dr. J. A. STEPHENS (Huddersfield) moved that the maximum number of patients allowable on a doctor's list should be reduced from 4000 to 3000. Dr. J. C. ARTHUR (Gateshead) deplored this outbreak of trades-unionism and restrictive practices. Provided a doctor was efficient and prepared to work hard, he could, unless his geographical circumstances were unsuitable, look after 4000 patients. To reduce the number would penalise the efficient and hard-working and also reduce the patient's freedom of choice. Dr. R. W. COCKSHUT (Hendon) thought that a case might be made out later for a maximum of 3500, but 3000 was dangerously near to putting all doctors on the same level. Dr. W. JOPE (High Blantyre) urged the meeting not to be ridiculous. The population was about 48 million, and there were 20,000 general practitioners. After making allowances for sparsely populated isolated districts and for elderly doctors, all young active practitioners would have to be prepared to look after 4000 for some time. Dr. W. N. LEAK (Cheshire) was concerned for the freedom of the doctors. The service was still too young for compulsion. It might, he agreed, be wise to reduce the limit later. The motion was lost.

BETTERMENT

A number of amendments proposing that 85% betterment should be asked rather than 70% were taken together. Dr. J. KENNEDY (Hampstead) spoke for many when he said that if they started at 85% they would have a fair chance of getting 70%. If Mr. Bevan called the doctors mercenary let them do something to prove it. Dr. G. DE SWIET (Paddington) thought the report might have been stronger if the figures for specialists' remuneration had been known at the time. Dr. D. L. S. JOHNSTON (Halifax) suggested that not to press for 85 showed a distrust in their own figures. At law you pressed for what you thought you should get, not for what you hoped to get. Dr. N. C. FLETCHER (Finchley) pointed out that the profession gave a 24-hour service and provided locums for holidays and times of sickness. But Dr. COCKSHUT reminded the meeting that allowance for practice expenses had already been made under the Spens recommendations. Under the service some expenses —notably drugs—had dwindled. If the Spens recommendations were accepted they must be accepted whole, and they laid down that the doctor's remuneration must be considered in relation to other professions.

Dr. LEAK thought they could not unduly stress underpayment while the medical schools were full to overflowing. He foresaw that the Government might soon be in difficulties, for everyone would want to be a specialist. The motion was lost.

Dr. A. BROWN (Cambridge and Huntingdon) proposed that if the Minister gave an increase of £10 million or over it should be used to increase the fee for the first 2000 patients. Who were the people with only 1000 patients, he asked. Those who were doing part-time work as specialists ; the older doctors, those with private means who chose only to do a modicum of work ; and lastly those in sparsely populated areas who could be helped in other ways. Mr. A. STAVELEY GOUGH (Watford) would have liked to see the cases of hardship analysed. How many were new practitioners, how many specialists ? If their aim was for each doctor to have 2000 patients they should make it economically attractive to have 2000 patients. Save in exceptional areas 1000 patients did not provide a reasonable day's work and the doctor with only that number on his list was not an economic proposition to the country. Dr. WAND put the case of the young doctor, and added that the basic salary would be needed less often if the fee for the first 1000 patients was raised. To raise it to 2000 would water down any help given. Dr. DAIN pointed out that people with small lists had proportionately high expenses. The motion was lost.

The chairman then announced that no amendment had been carried modifying the report in the form in which it had gone to the Minister; and the meeting approved the recommendation that the fullest support be given to the conference of Local Medical Committees in seeking an adjustment of general-practitioner remuneration on the basis of the report.

On the motion of Dr. DAIN, the meeting unanimously passed the following rider to the recommendation :

> That the representative body expresses its great concern that the Minister, having received the general practitioners' representations on the betterment factor more than two months ago, and the report by the general medical services committee on March 4, has not conceded the necessary adjustments to the pool to implement Spens at present-day values in time for the increased payments to be made in this quarter's payments. This delay shows disregard for the serious hardship now being experienced by many general practitioners in the service, and is seriously prejudicing its success.

RURAL PRACTITIONERS

Dr. G. H. EDGECOMBE (Westmorland) pressed, on behalf of rural practitioners, for a further increase in the sum allotted for mileage payments. In Westmorland, he said, the average number of patients on the list of each doctor (including those in towns) was 1400. The rural practitioner's work was increased by : (1) the inaccessibility of his patients ; (2) the lack of hospital outpatient departments ; and (3) the shortage of transport, necessitating visits by the doctor when otherwise the patient might attend for a consultation. Moreover, the rural doctor suffered in that the mileage allowance did not count in the reckoning of pensions. Dr. J. C. PEARCE, chairman of the rural practitioners' subcommittee, assured representatives that the distribution of mileage money would be discussed with the Ministry as soon as practitioners' claims had been received in full. The Westmorland resolution was carried.

1. *Brit. med. J.* Feb. 19, suppl. p. 83.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

THE most exciting event in last Saturday's broadcast play, *Duet for Two Hands*, was, naturally enough, the arrival of THE LANCET in Orkney. Next time the play is produced I hope we shall have fewer cries from the kittiwakes, and a longer extract from your leading article, which struck a new note; though it seemed a pity that the contributor you praised so highly should later turn out to be a murderer. In more cheerful vein was the previous week's televised version of the work of a casualty department, in which one of the casualty officers was made to say he thought of contributing a paper to your columns on Whisky and Wallop. From time to time both doctors picked up a copy of the journal; though I regret to say that on each occasion they put it down again very quickly. The "prop" department must have had an interesting time collecting such effects as angle forceps, medical reference books, and a bottle of barbiturate (found in a car?). But I still think it odd that the girl who had a sprained ankle should leave the hospital with one stocking on and one off.

* * *

The dangers that may lurk in one's own garden, even though *Atropa belladonna*, *Solanum dulcamara*, *Hyoscyamus niger*, and other poisonous plants have never been admitted, are disconcerting. I was pointing with pride to some fine ivy tods on the garden fence not long ago when my guest stopped disapprovingly and told me the following cautionary tale.

A few years ago a minister's wife and her young son of twelve were trimming ivy in their West Country garden. It was summer, and from time to time the boy refreshed himself by eating loganberries, which were growing nearby. Presently he complained of feeling unwell and the mother became alarmed; she put him to bed and sent for the doctor. The case seemed serious and urgent as well as mysterious, and the doctor immediately summoned a consultant from the nearest big town, about ten miles away. But as the consultant entered the room the boy died.

It was said that the highly acid juice of the loganberry combines with that of ivy to form a deadly poison. If this is true, it gives one to think furiously. Most gardens of any size grow loganberries and allied species, and most have ivy somewhere; that more accidents have not been reported may be because loganberries are not in season at Christmas. Ivy alone has a vague reputation of being poisonous, but this does not seem to be borne out by the books, and we know on good authority that little lambs eat it. The berries are said to be purgative, and the juice of the leaves used to be used as a dressing for ulcers [1]; the botanists do not mention toxic effects, and the author of my wild-flower book says the berries are dry, hard, and tasteless, as though he had sampled them.

It makes one wonder what other unsuspected incompatibilities there may be in the garden.

* * *

Early in 1941, while working in a boys' club, I came across a young lad who had been evacuated from a blitzed area, where his home had been bombed and his mother and young sister killed. When we knew him he was billeted with an old lady, who obviously did not want him and of whom he was rather afraid. One night after he had gone to bed she found him by the open window trying to jump out. He was referred by the billeting officer to the local child psychiatrist—a well-meaning woman, very keen on her work—with whom he had many sessions. These interviews seemed to have had little success, for the billeting officer asked us to do what we could to help the lad with his troubles. As far as we were concerned, he was a good club lad and the story of his attempted suicide came as a surprise.

One evening the club leader—an adept at putting boys at their ease—got him talking over the fire. First the lad told us the questions the "woman doctor" had asked: Was he unhappy here? Did he like his billet? How had his mother and sister been killed? Had he actually seen them killed? And many more. Then suddenly the whole story came out. He had not told anyone else because it was not the sort of thing you could tell strangers, and certainly not women. Apparently his bedroom was at the top of an old dark house and getting to the lavatory involved a long journey across a dark cold courtyard; and he concluded rather lamely, "the window seemed the obvious answer."

Several morals might be drawn from this story, but to me it provides yet another illustration of the weakness of the specialist, who is rarely in a position to know his patients as individuals.

* * *

After five years in a crowded city in the far north-west of China, England indeed seems a green and pleasant land. I have been "home" now nearly a week and have not seen a single person expectorate in public, have actually given my luggage over to a porter without needing to watch him with it the whole time, and have been to a hairdresser's without having to rush back for a disinfectant wash immediately afterwards. The streets of this busy northern town are incredibly clean to my China-accustomed eyes, and a qualm of guilty conscience assails me when I forget to place used tickets in the proper receptacle on the bus. It takes five years abroad to enable one to appreciate the kindliness of one's fellow-countrymen in the next street. I have never had so many folk out to oblige a stranger though they do not necessarily make anything out of it.

* * *

Alison is Canadian, but she has been with us long enough to be regarded as one of the family. While out in the woods with the children the other day she had a nasty fall, and when I returned home it was obvious she must go to hospital. "Will you take her to Sister Tussle?" plaintively inquired Janet, my four-year-old, for she has a very special regard for Sister Tussle, who can cure anything. I rang up, but Sister pointed out that Alison would be better admitted to one of the special centres. So, and not without trouble, next day Alison was taken to a special hospital. Janet was very worried that we had not sent enough clothes, and when I opened my bag later I found that another nightie and other things had been surreptitiously stuffed under my papers.

Progress was slow but uneventful, and at the end of three weeks I called at the hospital to collect Alison. She seemed well, and to my surprise the leg was not stiff. I saw she had strapping over the greater trochanter so I asked what had been done. "They've pinned it," I was told. I was surprised that this new generation of orthopædic surgeons should use even a modified Smith-Peterson nail on a two-year-old. As I left I remarked that this was the first benefit I had received from the National Health Scheme. "Unfortunately, sir, the benefits do not extend to all dependants," the secretary said. "Just what I thought," I replied, having myself spent all that day in the service of the State at another hospital. "What do I owe?" "One and sixpence," she said, and I paid gladly, feeling that there must at least be a State subsidy if that was all the Dolls' Hospital charged for fixing a leg on our dolly.

* * *

Your correspondent's story of the Swedish guide reminds me of other pitfalls which await the users of foreign languages. The German prepositions, which look so innocently like our own, are a good example, and among them I suppose none is more confusing than the German *bei*, which may mean, "near" or "at the house of," but never "by."

At the house of a friend one day I was introduced to a German lady who, though she had married an Englishman and lived in England for a good many years, had never mastered the subtle differences between the languages. In the course of conversation a Mr. Palmer was mentioned—the headmaster of the local preparatory school for boys. Hearing the name of someone she knew, she made haste to join in the conversation, saying "Did you say Mr. Palmer? I had a child by him."

1. See *Extra Pharmacopœia* of 1920, vol. I, p. 800.

Digitized by Google

Letters to the Editor

UNIVERSITY REMUNERATION

SIR,—As a whole-time member of a university staff with full clinical appointments, I read with alarm and dismay the proposals for the remuneration of specialists. Two discrepancies were immediately apparent. Firstly, the whole-time clinical staff in medical schools will receive remuneration according to the new scale from April 1, 1949, whereas all other branches of the service will be remunerated in retrospect from July 5, 1948; and secondly, such university clinical specialists will be rated financially at approximately £1000 per annum less than their whole-time purely clinical colleagues in teaching hospitals.

The first point defies explanation and the second apparently follows a tradition which can no longer be justified or maintained. Personally I feel that the proposed scales are quite unjust to those holding whole-time clinical posts in medical schools.

Edinburgh. G. DOUGLAS MATTHEW.

HÆMOGLOBINURIA

SIR,—I agree with Dr. Dacie (March 19) that Stats, Wasserman, and Rosenthal [1] are unnecessarily cautious in their advocacy of parsimony in blood-transfusion in cases of nocturnal hæmoglobinuria.

In the case of a woman of 33, who had suffered from this malady for some five years, hæmoglobin had been passed in the urine continuously for weeks before I first saw her; and her general condition was extremely poor.

Seventeen days ago her urine was port-wine colour before I commenced a replacement transfusion, during which 5½ pints of blood were drawn off, and 7 pints of citrated blood with 5 of concentrated corpuscles were given. Half-way through the operation the urine was brownish-pink, but two hours after the operation, although still turbid, the urine contained no hæmoglobin. Now it is still free from hæmoglobin.

My only reason for publishing this note at so early a stage is to support Dr. Dacie's assertion that blood-transfusion is not necessarily contra-indicated in nocturnal hæmoglobinuria; and to point out that we are no longer as therapeutically impotent as we were. At a later date, Dr. P. H. Willcox and I hope to publish a detailed study of our case.

London, W.1. A. PINEY.

THE UNDESCENDED TESTICLE

SIR,—Mr. Denis Browne's presentation, last week, of his illuminating work and views would not encourage the comprehensive objectivity he appears to miss in your annotation of the previous week. Clinical diagnosis can be sound whether or not his new anatomy should replace the older. If a testicle is palpable, few clinicians who see many cases will fail to decide correctly whether it is ectopic or not. If both testicles are not palpable, few clinicians will venture to predict whether or not there is a mechanical obstruction to their descent. If one testicle only is not palpable, it can perhaps be predicted with some confidence, though not with certainty, that there is such an obstruction.

If gonadotrophins produce descent of testicles into the scrotum, then obviously there was no mechanical obstruction to their descent. If they fail to do so, the opposite conclusion is admittedly less certain. As to the alleged danger of overdosage, chorionic gonadotrophins are usually used, and I know of no practical danger of overdosage and certainly none of injury to the testicle. Testosterone or methyl testosterone is occasionally used; this is less effective, and its use involves the danger of producing sexual precocity, and possibly some temporary involution of the testicle, if therapy is too intensive or prolonged.

Endocrinologists and surgeons are agreed that some 75% of "undescended testicles" will descend spontaneously at puberty, and both endocrinologists and surgeons (according to Mr. Browne) treat such cases, by hormones and surgery respectively, before puberty with effective results. Of course the surgery is not justified, and Mr. Browne is doing good service to surgery by frequently saying so. As to hormone therapy, I pointed out at the Royal Society of Medicine discussion that chronological puberty is not identical with physiological puberty; and many of these patients do not attain physiological puberty until their late teens. If this happens, or if their endocrine pattern suggests that this will happen, it would appear to me that hormone therapy is well justified to accelerate a process that might occur spontaneously at a belated time. The other reason for hormone therapy is excessive anxiety of the patient and the parents about the absence of the testicles from the scrotum in contrast with other boys, especially at boarding-schools.

It seems a pity that this relatively simple overlapping branch of endocrinology and surgery should be unnecessarily complicated by over-elaborated controversy.

London, W.1. S. L. SIMPSON.

OPTICIANS AND PHARMACISTS

SIR,—In reply to Mr. Giles (March 12), I should like to say that I was quite aware of the standards of examination required by the British Optical Association. The association is, however, not the only body which grants a registrable qualification in optics; other examining bodies do not require such strict standards from intending candidates, and courses of study for these examinations can be completed on a part-time basis.

For the pharmacist there is only one body empowered to grant registration—the Pharmaceutical Society of Great Britain. For a considerable number of years the minimum standards of training recognised by the Pharmaceutical Society have been 2 years' full-time study with a practical training of 2 or 3 years.

London, W.9. ARTHUR G. SHAW.

VITAMIN B_{12}

SIR,—Your leading article of Jan. 22 contains the following statement:

> "... but we know that liver extracts, particularly the more purified types, have at best only a partial effect on the organic signs and symptoms of those patients with subacute combined degeneration who have no significant anæmia ..."[11]

This statement suggests that it has been demonstrated that liver extracts of less purified type are for some reason more effective than are those of greater purification in the control of the signs and symptoms caused by subacute combined degeneration of the spinal cord. Such a statement is not supported by the facts available and should be corrected because of its misleading implication in respect to the highly refined and potent extracts available, which are still the treatment of choice for patients with pernicious anæmia with or without combined-system disease. The amount of improvement in the signs and symptoms which will occur as the result of treatment varies considerably, depending on a number of factors which need not be re-enumerated here; but it is unfortunate that statements of this sort, made at first carelessly, and not based on the results of controlled investigation, should be quoted as fact.

Boston, Mass. WILLIAM P. MURPHY.

*** We are grateful to Dr. Murphy for drawing attention to this point, on which the article was insufficiently explicit. The suggestion that the less highly purified liver extracts should be used in the treatment of neurological complications of pernicious anæmia finds some support in textbooks. For example, Wintrobe (*Clinical Hematology*, 2nd ed., p. 328) says:

> "... for patients with involvement of the central nervous system it has been recommended that whole liver and crude extracts of liver, rather than refined, be used; in the process of concentration, factors necessary for the nervous system may be unknowingly lost or destroyed. For this view there is little evidence. Nevertheless, since so little is known about the cause of the lesions in the central nervous system, it seems wise to ensure a plentiful supply of nutritive factors."

Our article dealt with: (1) subacute combined degeneration without significant anæmia, which is

1. Stats, D., Wasserman, L. R., Rosenthal, N. *Amer. J. clin. Path.* 1948, 18, 757.

Digitized by Google

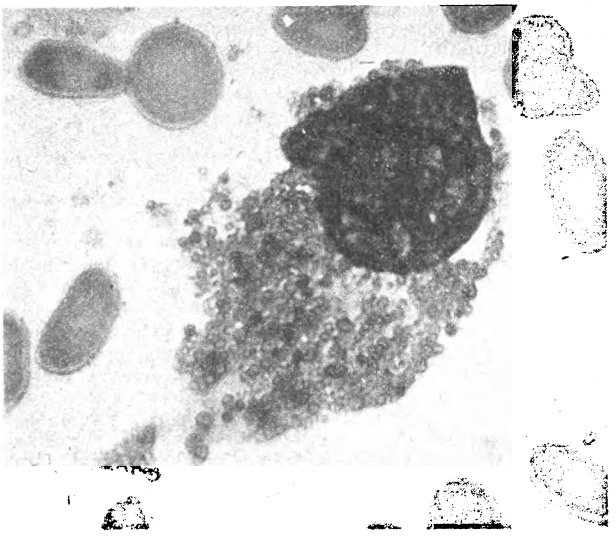
notoriously resistant to treatment; and (2) purified liver extracts. Here it should have been indicated that we had in mind those prepared by the technique of Dakin and West and other similar methods; we were not referring to the concentrated "refined" extracts which are popular in the U.S.A., but which we are not allowed to import.—ED. L.

THE EOSINOPHIL CELL

SIR,—According to Duran-Jorda [1] the granules of the eosinophil cells are round in man and many other mammals, whereas in the camel they are oval. It is well known that the mature erythrocytes of camels and llamas are oval or elliptical, whereas their immature red cells found in the bone-marrow are round. Duran-Jorda considered his observation to prove his earlier view that erythrocytes are derived not from immature red cells through maturation of erythroblasts but from the eosinophil granules. In his opinion the assumption that human round eosinophil granules are converted into round erythrocytes, and oval granules in camels to oval erythrocytes, is more likely than the assumption that round immature red blood-cells turn into oval erythrocytes.

In 1946 J. Matsch and I published data concerning two elliptocytic families.[2] The erythroblasts of the bone-marrow of elliptocytic people are round, whereas in the peripheral blood more than 25% of the red blood-cells are elliptical. In some cases observed by us the elliptocytes in the peripheral blood were more than 90%. In one of the two families (four generations were reported) cases of severe hæmolytic anæmia occurred. In three of the brothers and sisters the hæmolytic anæmia was so severe as to need splenectomy. After splenectomy the degree of hæmolysis has become normal in all three patients, the anæmia has ceased, and erythropoiesis, which was increased in the bone-marrow, has now become normal, like the resistance of the erythrocytes and the number of reticulocytes. During the hæmolytic stage the thickness of the erythrocytes was greater (3·3 μ); after splenectomy their thickness became normal (2·2 μ). The elliptocytosis remained unchanged. The result of the operation lasted 7–18 years. As regards heredity, the parents were cousins: one of the paternal grandparents was the brother of one of the maternal grandparents. Elliptocytosis was transmitted from the maternal side, this maternal grandparent being the partial carrier of the anomaly. On the paternal side hæmolytic anæmia also was probably transmitted, because 14 brothers and sisters of the father, who was already dead at the time of examination, had died in early childhood, very likely of hæmolytic anæmia. We inferred that elliptocytosis and a hæmolytic tendency had been simultaneously inherited. The increased thickness and diminished resistance of the elliptocytes were secondary to this hæmolytic mechanism. Otherwise it could not be explained why splenectomy—i.e., the removal of the central organ of this system—led to normal cell thickness and regression of the hæmolytic phenomena, while the erythrocytes remained elliptical. In our patients it was in the reticulocyte stage that round and elliptical cells were found at the same time.

1. Duran-Jorda, F. *Lancet*, 1948, ii, 451.
2. Lendvai, J., Matsch, J. *Orv. Lapja*, 1946, **2**, 445.



The shape of the eosinophil granules is interesting. The accompanying figure shows a slightly damaged myelocyte, found in the bone-marrow, and its eosinophil granules, which are round, whereas the erythrocytes are elliptical. In this patient over 90% of the erythrocytes were, as in the camel, elliptical by heredity, whereas the eosinophil granules were not elliptical but round. We believe that the conclusions drawn from the similarity of erythrocytes and eosinophil granules have been erroneously applied to human erythropoiesis, the shape of the erythrocytes and the granules being different in our patient.

Budapest. J. LENDVAI.

ROAD ACCIDENTS

SIR,—Your correspondents on road accidents have not mentioned dogs as a factor. Some months ago I wrote to the R.A.C., suggesting that research should be initiated on the reactions of dogs to road vehicles.

It is the experience of every motorist, at times, to sound the horn vigorously, and the dog still stands in the middle of the road. I wondered whether this may be due to tone-deafness at the frequency of the ordinary motor-horn. I suggested to the R.A.C. that they might investigate this question, and produce a horn possibly inaudible to the human ear but offensive to a dog's ear, rather on the lines of dog whistles which are of such high frequency that the human ear cannot detect them. Furthermore, large-scale research should be undertaken on the general reactions of dogs to motor vehicles, with a view to finding some offensive instrument which would frighten them from the road. I think the figures show that the stray dog is as much responsible for accidents as the other factors, but I have seen no evidence that this problem is being seriously studied.

Urmston, Lancs. B. SANDLER.

MYASTHENIA GRAVIS

SIR,—Having seen the account of myasthenia gravis in your issue of Jan. 29, by a contributor to the Disabilities series, I feel that my own experience of this disease may be of interest.

The trouble started at the end of 1942 when I was aged 22, and the first symptoms were, in my case also, imbalance of the eye muscles resulting in double vision. Within three months, excessive fatigue became apparent, and I found myself unable to continue with my fairly light manual job.

Unlike your contributor, however, I experienced no variations in the rigour of the symptoms, my decline in strength steadily progressing until I was sent into hospital. There I had an injection of 20 mg. neostigmine bromide with dramatic results, and shortly afterwards I was discharged with instructions to take three 15 mg. tablets by mouth daily, together with ephedrine gr. $^1/_2$.

It soon became clear that my steady decline in strength was continuing, the tablets only affording very temporary relief; and after consultation with another neurologist, and increasing the dosage up to nine or ten tablets per day, I decided to try deep X-ray therapy to the thymus gland. The eight-week course of treatment was finished about the end of August, 1943, and a fortnight later I came to the conclusion that my decline in strength had been checked.

At this stage I was taking the maximum dose of neostigmine; I could walk about 100 yards if the going was smooth; I could open my eyes about half-way for short periods with difficulty; I could talk for about one minute; grimaces were impossible; and I was having considerable difficulty in swallowing solid food. From this time on, my improvement, though slow, was steady. Gradually I was able to reduce the dose of neostigmine until finally it became unnecessary. In the spring of 1944 I started a part-time clerical job, and was subsequently able to resume full-time clerical work.

In 1946, however, much to my dismay I had a recurrence of the diplopia, and gradually my old symptoms began to

Digitized by Google

return. I was told that there was a possibility that the deep X-ray therapy had left some small part of the thymus still active, and that it had regenerated. Accordingly, during the winter of 1946–47, I again underwent a course of this therapy, and the skin reaction on this occasion was somewhat more marked.

My recovery since then has been very satisfactory. Certain of the small muscles of my hands are still extremely weak and become rapidly fatigued, making it impossible for me to carry a heavy suitcase or grip a tennis-racquet satisfactorily; but a twelve-mile hill walk is not outside my capabilities, and my general health is good.

FELLOW-SUFFERER.

ON GETTING WARM

SIR,—A fair number of older people have to get up during the night, especially in cold weather, and some of them find it difficult to get warm again in the intervals. I suppose it is a matter of common knowledge (despite the trend of modern education) that warm-blooded animals get most of the heat they need from their voluntary muscles, which act as slow-combustion stoves, or immersion-heaters. But I find it is less well known, even by doctors, that by tensing one set of muscles against their opponents, especially those of the lower limbs, it is possible to warm up the whole body quickly, with practically no movement of the parts concerned nor disturbance of the bedclothes. Some years ago I learned that Arctic explorers shivered in their sleeping-bags till they got warm. But the method I have described is much more efficacious.

Bolton. R. D. MOTHERSOLE.

HOSPITAL ADMISSIONS

SIR,—The growing difficulty in obtaining admission of patients to hospital may, I suggest, be due partly to the change in administration which took place on July 5. Previously, municipal hospitals admitted patients from definite areas; but such demarcation no longer exists, and in theory a patient could now be admitted to any hospital in the country.

Under the old system a municipal hospital was able to allocate wards according to the needs of the population, and it was almost unknown for an acute case to be refused admission. Under the new conditions, however, the hospital finds it difficult to decide what type of patient to admit. For example, should an acutely ill patient 20 miles distant be given a bed in preference to a waiting-list patient who lives only 20 yards away? The mileage covered by the ambulance service in the Manchester area has doubled since the new service started, which must mean that some patients are travelling great distances to hospitals willing to accept them.

Complaints are being directed against the hospitals because they will not admit the acutely ill when their beds are already fully occupied or when one or two beds are being kept for local emergencies. Thus hospital administrators may soon be driven to accept on demand any patient from any distance so long as a bed is available; then, when all the beds are full, the doors will be closed and no patient, however ill, will be accepted.

It seems that the solution may lie in some form of rationing. The first step will be to determine the number of population per hospital bed, excluding the special hospitals dealing with patients on a regional basis. The beds will then be allocated according to the number of the local population they have to serve; and each hospital, or group of small hospitals, will be responsible for providing a complete service to its own population. In such a hospital, or group, beds will be divided according to local demand for different types of accommodation; thus proportions will be allotted to general surgery, general medicine, chronic sick, emergencies, and so forth.

There will be nothing to prevent a patient on a hospital waiting-list seeking admission to a hospital in any region. The number of beds available to various groups of waiting-list patients should be made known to general practitioners by informing them periodically about the length of the list in each group at each hospital, which would enable them to advise their patients accordingly. The chief advantage of the system, however, would be that each hospital would have the duty, and opportunity, of providing for all urgent demands from its own local population. Every emergency call would be accepted.

Withington Hospital, Manchester. J. M. GREENWOOD Medical Superintendent.

ESTIMATION OF DIAMIDINES IN BODY FLUIDS

SIR,—The aromatic diamidines are now firmly established in clinical practice. They were originally introduced for the treatment of certain protozoal diseases, but recent work has shown that they can be of value in microbic infections as well. Detailed studies on their clinical use have, unfortunately, been somewhat handicapped by the absence of a reasonably convenient method of estimating concentrations in body fluids during treatment. It is, of course, obvious that the effective concentrations obtained in the human subject during treatment are so small that easy estimation without inaccuracies may be difficult. I am therefore venturing to bring to your notice a new technique for their determination by means of Fearon's penta-cyano-ammonio-ferrate reagent,[1] described hereafter as the P.C.A.F. method. This has been used for estimating propamidine and dibromopropamidine.

The P.C.A.F. reagent gives a specific yellow-to-orange coloration with distilled-water solution of the diamidines mentioned above, in vitro, and also gives the same colorations with protein-free blood-serum solutions from patients who are being chemotherapeutically treated. The colorations of these solutions have been proved to vary quantitatively with their diamidine content; thereby standard calibration curves of the drugs themselves can be prepared, and then the unknown blood-serum diamidine level can be determined from these curves. The actual estimation takes about an hour from the arrival of whole blood in the laboratory, and the determination can be carried out in one ordinarily equipped with a 'Hilger Biochem' colorimeter.

A serum blank must be obtained from blood drawn from the patient before treatment commences. Its value must be determined so that corrections can be made in the readings with specimens obtained during treatment. Further, it still has to be decided whether spontaneous variations normally take place.

Further details of the method will shortly be published.

Dudley Road Hospital, Birmingham. H. TROUGHT.

ARTIFICIAL INSEMINATION

SIR,—The attack launched upon the Medical Defence Union by the Archbishop of Canterbury and by Lord Merriman during the Lords debate on artificial insemination,[2] appears to be misdirected and perhaps due to a failure by each of them to appreciate the function and services of that body. It is possible that they may labour under the conviction that the Union sponsors or advocates a particular line of treatment such as artificial insemination. This is not so. The decision as to whether artificial insemination will constitute appropriate treatment for any given patient rests within the judgment of the doctor in attendance. He and he alone can determine whether or not it is fitting and proper to recommend that line of treatment to remedy a sterile marriage.

The Union, fulfilling a primary function defined in its memorandum, has consistently warned its members in a suitable manner of the medicolegal dangers associated with artificial insemination. It has pointed out that they may be accused of negligence, of adultery, or of conspiracy. It has shown to those who desire to undertake this form of therapy the precautions that they should adopt, and it has published two documents which it has been advised by its solicitors are suitable for completion by the parties concerned. It holds no brief for any person who knowingly commits perjury at the time of the registration of the child that is the result of A.I.D.

If the Archbishop's commission had afforded the Union an opportunity of appearing before it when it was in session, it is just possible that the persons appointed to give evidence on its behalf would have

1. Fearon, W. R. *Analyst*, 1946, **71**, 562.
2. See *Lancet*, March 26, p. 540.

Digitized by Google

removed some of the unfortunate misapprehensions that appear to have arisen in their minds.

The law may require alteration, but this, if necessary, should only be effected after the matter of artificial insemination has been fully explored by a Royal Commission or a departmental committee. It would be unfortunate if the Church were once more to align itself with the opponents of a new form of therapy until that therapy has been properly examined by competent authorities and either condemned or confirmed.

Medical Defence Union,
49, Bedford Square, London, W.C.1.

ROBERT FORBES
Secretary.

MEDICAL EDUCATION

SIR,—The health of the people and the improvement of the age-structure of the population require that the number of doctors should be increased considerably. For a satisfactory health service the number of registered doctors must at least be doubled; and this necessitates a radical reform of the medical curriculum.

I believe that eventually one doctor to every 500 people will be required. On this basis the U.K. would require, instead of the present 50,000 registered practitioners, at least 100,000. The achievements of medical research do not alter the fact that in the last resort the practice of medicine is an art, which is based on observation and whose foundations are empirical. For this reason the bias of medical education must be made essentially practical—at any rate during the early stages—since associated sciences, such as physiology and anatomy, cannot become fully intelligible to the student except through their practical application.

Thus in the scheme for a reformed medical education which I wish to outline here, all students would start by acquiring the foundations of practical medicine as rapidly as possible; and this primary stage would take place in medical schools. I would urge that every hospital with more than, say, 200 beds should, when properly adjusted for teaching, be used as a medical school. The monopoly of instruction by the present teaching hospitals is quite unjustified. It is a commonplace that doctors overrate themselves and underrate their colleagues, and the same is true of the teaching hospitals, especially in their attitude towards those who practise their art in smaller and less privileged institutions.

It is my firm conviction that the fundamental elementary teaching of the general practitioner can be carried out by young qualified men, ambitious to prove their worth, at least as well as by older, tired men. In fact this happens today when "coaching" is entrusted to young assistants. The experience of older men will be used to best advantage in clinical instruction. If all the clinical material were used to the full, patients need be disturbed for examination less than they are now at existing teaching centres.

Large amounts of useless theoretical knowledge, acquired today at the cost of much time and energy, must be jettisoned. Practitioners should learn only what is of practical use to them; the teaching should be factual and should not concern itself with current problems. Once and for all the medieval preoccupation with anatomical detail must be eradicated. The time consumed in learning structural details which the practitioner does not and cannot use would be spent much more profitably on practical questions. The same holds good for much of the teaching in physiology. The amount of physics, chemistry, botany, and zoology required at this stage of the training could also be cut down considerably, leaving just enough to inform the student of the relation of these branches to practical medicine. The suggested reduction of the subject-matter to the minimum would enable the student to proceed to clinical work much earlier, and would also enable him to qualify in four years instead of the present six.

It must be remembered that this scheme is intended for the training of practitioners. Once they have completed this training they must have the opportunity of specialist training. This, I suggest, should be the special concern of the privileged teaching hospitals, which must be staffed by highly trained and experienced doctors and equipped with up-to-date laboratories. In these special hospitals the aspiring specialist or consultant must of course have the opportunity to develop his special subject to the highest level of scholarship. Whereas today anyone can call himself a consultant, in future only a physician who has proved his ability in this field should be entitled to do so.

The third category of students are the aspiring research-workers. Most of them, though by no means all, will have graduated from the specialist schools. It is most important that workers, wherever they may come from and whatever their qualifications, should not be debarred from research work. Many of the greatest advances in medical science have been made by men who were very mediocre doctors. Those students who show a talent for research and have original ideas worth pursuing and elaborating, and the ability to develop them, should have the chance of serving an apprenticeship with a master of research. Wherever possible these should be concentrated in special research institutes remote from the distractions of cities.

We may summarise these suggestions by saying that medical training should be subdivided into three parts to be carried out respectively in (1) medical schools, (2) teaching hospitals associated with universities, and (3) research institutes. The most important feature of my suggestions is the separation of the indispensable practitioner from the scientist, and then the radical revision of the curriculum. Thus we may fulfil the categorical imperative of our time—to create the necessary number of practitioners, and simultaneously to protect and stimulate the development of medical science.

In reality my plan amounts to a systematic reorganisation of the medical profession along the lines of its historical origin in Europe: the barber-surgeons, the more learned doctors, specialising in certain chosen disciplines, and the searching pioneers.

London, W.1. JOHN PLESCH.

SYSTOLIC MURMURS

SIR,—Your annotation of March 19 prompts me to mention a tip given by a correspondent in your journal many years ago, which still does not appear to be generally known. Firm pressure of the stethoscope against the chest wall will cause a functional murmur to disappear, whereas an organic murmur is unaffected. Of course it is not claimed that this test is infallible, but I have always found it a very good guide. I am sorry that I cannot remember the name of the clinician who first described it.

H. C. B.

CRASH HELMETS

SIR,—All adults, particularly parents, to whom I have spoken agree fervently with my suggestion that motor-cyclists should wear helmets.[1] All, or nearly all, adolescents consider me a pessimistic bore, since they see no possibility of any accident happening to them.

Mr. Warburton, in his letter of Feb. 26, argues that the wearing of crash helmets would foster a false sense of security; but even so, this would soon wear off; and headache does not come on quite as early as he suggests (after 30 miles). The hazard of impaired road judgment through headache is very real however.

The *Motor Cycle* of Jan. 27 contains a plea for a better-looking, cheaper, and more comfortable crash helmet—a sign that all is not well with existing ones. Mr. C. Reid, of Messrs. Grant & Irving, Dumfries, suggests a pith one like the tropical topee; its shape would have to be altered, for otherwise rider and helmet would soon part company. Is it the weight or the lack of ventilation which makes the Service helmet uncomfortable? The heaviest part is the rubber; this might be replaceable by springs of drawn phosphor-bronze. Ventilation presents little difficulty. The issue of helmets with motor-cycles would give the movement a great boost; I am collecting the names of firms willing to supply them with new machines.

In my investigations I have been impressed by the danger of faulty cambering at bends on hills and at corners. If the R.A.C. and A.A. were to give suitable warnings, many accidents would be avoided.

The reticence of insurance companies regarding rates is ominous. In these days when one is urged to insure

1. *Lancet*, Jan. 22, p. 166.

Digitized by Google

against everything, including twins, why do they discourage motor-cyclists from insuring themselves against accidents? Or when they accept, why do they charge exorbitant premiums?

Maxwelltown, Dumfries. A. P. BERTWISTLE.

CORONARY THROMBOSIS

SIR,—May I comment on Dr. Evans's assertion, reported in your annotation last week, that morphine is the supreme anodyne for coronary thrombosis? Working as a general practitioner, I have twice seen death occur within ten minutes of the *relief of pain* by an injection of morphine for coronary thrombosis. Is there any explanation of this phenomenon?

London, N.W.3. L. V. SNOWMAN.

HEALTH CENTRES

SIR,—Your account (March 12) of the discussion on health centres held at the Royal Society of Medicine is concerned mainly with accommodation for general-practitioner services. The main purpose of a health centre, however, should be to promote a higher standard of health among the population it serves, and this requires the integration of the services of the regional hospital board, the local health authority, and the executive council—i.e., the marriage, now long overdue, of preventive and curative medicine. Those doctors who follow exclusively either the curative or the preventive branch can learn much from each other in consultation.

On the clinical side it is important that specialists should visit the centre for consultations, both to advise the general practitioners in particular cases and to bring the newer knowledge to those whom work prevents from attending postgraduate courses. Too little has been said, also, about the possibility of using health centres for the collection of valuable health and sickness records.

Hampstead. P. A. TYSER.

EXCHANGE CONTROL MEDICAL ADVISORY COMMITTEE

SIR,—I have recently had some correspondence with the Financial Secretary to the Treasury (the Rt. Hon. W. Glenvil Hall, M.P.) on the functioning of the Exchange Control Medical Advisory Committee, and I have his permission to send you the following extracts from his letter, in the hope that the explanation given and the statements therein made will help to clear up a certain amount of misunderstanding about this committee.

"The Exchange Control Medical Advisory Committee has no powers to make grants of any kind. What it does is to advise the Treasury on all applications for health treatment abroad, and it recommends whether or not the necessary foreign currency should be provided. It has nothing to do with who puts up the sterling to meet the expense.

"In practice, the majority of the cases with which the Committee deals are tuberculosis cases, and most of the members of the Committee (which is a panel of independent consultants) are, in fact, leading tuberculosis specialists. So far as tuberculosis cases are concerned, the great majority of all applications which come before them are approved. The approximate figures since the Committee was set up in December, 1947, are 1000 approvals out of 1100 applications.

"The way that the Committee works is that any sick person in this country can apply through his own doctor to the Committee. The doctor furnishes full medical reports and these reports are considered by two members of the Committee, and, in the event of their disagreement, by the Chairman as well. The criterion under which the Committee works is that treatment abroad must be essential to the recovery of the patient's health, and that such treatment cannot be obtained anywhere else in the Sterling Area. How this works out in practice is, of course, for the Committee to decide; but, as I understand it, the Committee would not normally approve applications in cases of tuberculosis which were too far advanced for treatment abroad to hold out any hope of recovery. I am sure you know, in certain types of case, high altitude would do more harm than good by causing the disease to flare up. In any case it would be a disservice to the country, and no kindness to the patient or to his family, to allow a sufferer to go abroad and to incur extremely expensive treatment in foreign sanatoria with no hope of ultimate recovery."

"I think you can take it that the Committee takes its duties very seriously, and that its members will always give the application the benefit of any doubts they may have. I feel confident that in any case where the Committee thinks that the patient has any real chance of recovery by going abroad, currency will be provided. Of course, even leading tuberculosis specialists may make mistakes, but I think it is also fair to say that the members of the Committee are as a rule in a better position to judge from the general nature of the case whether or not treatment abroad will be beneficial, than is the doctor who puts forward the application. It would be clearly impossible for the Committee to see the patients themselves, nor is it their function to do so; but if they are in any doubt they are at liberty to ask the doctor for further information, and they do not hesitate to do so."

House of Commons. WALTER ELLIOT.

SPECIALIST APPOINTMENTS

SIR,—I was interested to see, by your leading article of March 19, that you feel that, owing to growing demands on hospitals, the number of trainee specialists should not be reduced. Would you care to elaborate this view a little further? Is it not based on an impression? If it is not, hundreds of fully trained "trainee" physicians and surgeons will give a sigh of relief.

For the past two or three years there has been not one sign or symptom to suggest an officially recognised need for increased numbers of specialists. Anyone who, like myself, has been reading his LANCET as the Hebrews read their prayer-book—namely, from behind forwards—will tell you about the proverbial 5 fingers of one hand as far as numbers of recent advertisements for trained (not trainee) specialist posts are concerned.

For a large number of men and women belonging to the species of eternal registrar it has, for many months now, been a question of giving up or hanging on. It is quite obvious that a redistribution of available specialists can and must solve the problem. Can you assure us that this is being officially considered? Are new openings being created—and when? If not, do not raise the hopes of many who, after years of devoted and not unsuccessful apprenticeship (recognised at least in the R.A.M.C. by a majority), are exasperated by vague promises that they will eventually come into their own in the new service.

REGISTRAR.

*** Many more specialists are needed and it would therefore be a misfortune if financial cuts reduced the number of trainees. As our correspondent no doubt knows, it was decided that, except in cases of obvious urgency, new appointments should not be advertised until the reviewing committees of regional hospital boards and boards of governors have determined (*a*) the status of individual specialists at present working in the hospitals, and (*b*) the establishment needed to provide an adequate service. The work of these committees is to be completed before July 5.—ED. L.

". . . for the majority of this precious class of thinking men and women there does exist this overriding problem: how to be happy though well-informed. All around them they see headlines, dust-covers on books, posters, programmes of talks which cajole them into interest; not in the kind of problems that can be solved by private reflection, but the kind that demand the entire attention of large numbers of people for a long time everywhere. . . . In economic terms, of course, the issue is simple. Too many problems are chasing too few minds. As there is no immediate prospect of increasing the number of minds, there must be an attempt to decrease the number of problems. That is less difficult than it sounds, for no situation becomes a problem until someone makes it into one. If the thinking men and women made a great effort of self-denial, cut themselves down to a few problems a lifetime and held the rest at bay, the posers would be forced out of business. A sturdy refusal to be perplexed can work wonders for the well-informed who want to be happy."—*Economist*, March 12, p. 453.

Digitized by Google

Medicine and the Law

Surgeon's Successful Appeal

THE Court of Appeal reversed on March 21 the decision of Mr. Justice Birkett [1] which awarded £6300 damages against a surgeon for what was alleged to be a negligent diagnosis. The facts may be briefly recalled. Mr. Whiteford, an American engineer practising in England, complained that in 1942 he consulted a practitioner and a surgeon (Dr. S. R. Gleed and Mr. J. B. Hunter) and underwent operations on March 22 and April 5, and that he was informed that he had cancer and had only a short time to live. He said that, in view of that diagnosis, he wound up his practice and returned to America to die; in New York, however, he took fresh medical opinion and it was found that he was suffering not from cancer but from chronic cystitis and a considerable bladder diverticulum. The defendant surgeon denied liability. He admitted having diagnosed a cancerous growth in the bladder, but he pleaded that he did so after a careful manual and visual examination of the bladder and after taking all steps reasonable and practicable in the circumstances to check his diagnosis. The defendant practitioner (against whom the action for alleged negligence was dismissed by Mr. Justice Birkett) contended that he was acting under the surgeon's instructions at the two operations.

The law does not assume that medical practitioners guarantee accurate diagnosis. It is not every slip or mistake, observed Lord Justice Asquith in delivering the judgment of the Court of Appeal, that constitutes negligence. It was contended on behalf of the plaintiff that Mr. Hunter had been negligent in not verifying his diagnosis either (1) by cystoscopy or (2) by biopsy. In finding for the plaintiff, Mr. Justice Birkett had accepted both these contentions, basing himself upon the testimony of the American urologist, Dr. Barringer, whose evidence had been taken on commission. The Court of Appeal took a different view of the contentions. At the operation on April 5, 1942, it had been decided to open the bladder; this made cystoscopy entirely unnecessary. As for the biopsy it had been argued that this should be undertaken in every case where the presence or absence of cancer was in question. Mr. Hunter had given three reasons for not resorting to biopsy; these reasons were put to Dr. Barringer, but there is an inherent difficulty in taking evidence on commission and the Court of Appeal found his answers "obscure and ambiguous." It was not the fault of the witness in America or of the examiner who put the questions to him that there were, in Lord Justice Asquith's words, "ambiguities and gaps." The result was that Dr. Barringer's evidence did not satisfy the Court of Appeal as it had satisfied Mr. Justice Birkett last July. If there was nothing left of the contention about the omission to examine by cystoscope, and if it was not established that Mr. Hunter was negligent in omitting to carry out a biopsy, then the allegations of negligence disappeared and the defendant surgeon's appeal succeeded.

Common-law judges are accustomed to evidence being elicited orally in open court by the threefold process of examination-in-chief, cross-examination, and re-examination, during the normal course of the trial, so that any material point can be put to the material witness as it takes shape in the course of the trial. The taking of evidence outside the country, in advance of the trial, may be inevitable; but in Whiteford *v.* Hunter, where the plaintiff sought to establish his allegations of negligence by a witness whose testimony was taken on commission, there was this special feature. The Court of Appeal is always reluctant to take a different view of the value of evidence from that taken by the trial court; normally the trial court has seen and heard the witness and the Court of Appeal has not. As, however, Dr. Barringer's evidence was taken on commission in America, the trial court had no advantage over the Court of Appeal. The Court of Appeal had not seen or heard the witness, but neither had Mr. Justice Birkett.

The decision of the Court of Appeal is not the last word in the case, for leave has been granted for an appeal to the House of Lords. Although the supreme appellate tribunal may not throw much light on the technical issues of professional negligence in Mr. Whiteford's case, its final conclusions are sure to be of general interest.

1. See *Lancet*, 1948, ii, 232.

Gestation Period and Legal Inferences

In Jones *v.* Jones, a divorce petition heard before Mr. Commissioner Blanco-White on March 24, the period of possible gestation has been extended beyond any previous precedent in the courts. The husband contended that his wife must have committed adultery in his absence, since otherwise the period of pregnancy would have been 360 days. In a note on the Hadlum case [1] last year the periods previously accepted were discussed. In Gaskill *v.* Gaskill the time was 331 days.[2] In the Wood case it was 346,[1] in the Hadlum case 349. In the Jones case the period was 360 days. In this series of extensions the courts are still refusing to say that there is some line to be drawn beyond which it becomes impossible that the husband could have been the father of the child and in consequence an irresistible inference of adultery on the wife's part is set up.

The question, said the Commissioner in the recent case of Jones *v.* Jones, is whether the addition of 14 more days to the period of 346 accepted by the Divisional Court in Wood *v.* Wood in 1947 "is such as to tip the balance between a reasonable and a fantastic doubt." Adultery, he added, has to be proved beyond a reasonable doubt. The wife satisfied him that she was a respectable woman: "I don't think it right to condemn her on speculation; I am not satisfied beyond reasonable doubt that adultery has been committed."

Public Health

Mineral Oil In Food

THE *Manchester Guardian* (March 10) reports that a confectioner was fined by the Manchester magistrates for putting mineral oil into cake mixture. The Bench remarked that this was the fourth case in the city, and asked the trade organisations to tell their members once more that this practice is illegal.

Cakes made from a mixture containing mineral oil look better, have a better texture, and are heavier than those made with the limited amount of food fat that is at present permitted. The temptation to enrich mixtures in this way is understandable, but press reports make it clear that not only medicinal paraffin but also crude oils suitable for motor-car engines have been added. Confectioners who use these oils either for mixtures or for lubricating the cooking-tins can be prosecuted for selling a food "not of the nature, or of the substance, or of the quality, demanded"; for selling as a foodstuff a material that is not a foodstuff; or for contravening the Petroleum Act—which seems to be financially the most damaging charge.

Six years ago the Council on Foods and Nutrition [3] of the American Medical Association drew attention to the increasing use of liquid paraffin for salad oils and dressings, and for cooking chipped potatoes. Several workers had shown that continued ingestion of such oils interfered

1. *Lancet*, 1948, ii, 123.
2. *Ibid*, 1921, ii, 357.
3. *J. Amer. med. Ass.* 1943, **123**, 967.

Digitized by Google

seriously with the absorption of vitamins A, D, and K, and of calcium and phosphorus. Stryker [4] fed rabbits with mineral oil, some of which was shown histologically to have found its way through the intestinal wall into lymph-nodes. Frazer, Stewart, and Schulman [5] pointed out that mineral oils could be absorbed if thoroughly emulsified in the bowel; bile salts, oleic acid, and glyceryl monostearate sometimes occur together in the bowel, and then (they said) the proportion of liquid paraffin absorbed was of the same order as that of olive oil. Javert and Macri [6] described the case of a pregnant woman whose low blood-prothrombin concentration was traced to the habitual use of liquid paraffin; despite treatment, the child's prothrombin was also low at birth. In the face of such evidence, the council recommended that preparations containing mineral oils should be properly labelled and should be used only under medical direction.

This advice does not seem to have been heeded in the U.S.A.; for in 1947 the increasing use of mineral oils in food was again condemned.[7] Last year in this country, the *British Medical Journal* [8] reviewed experiments by A. C. Frazer and his co-workers. This time the question of carcinogens was raised, because heated paraffin contains oxidation products with fluorescent spectra resembling those of known carcinogens. In animals fed with heated oil no new growths resulted, but this negative evidence is perhaps not conclusive. The journal also recommended that liquid paraffin should be taken only on medical advice, and condemned altogether the use of unrefined mineral oils. Recently Coppock and Cookson [9] have reported that if thoroughly mixed into bread dough, a mineral oil forms a layer round each starch particle; whereas when the oil is used to lubricate the baking-tin, it forms a thin layer over the dough and is slightly absorbed during baking but it is not dispersed into droplets. Experiments designed to reproduce the processes of digestion suggested that the oil remained with the undigested residue or roughage, even when the emulsifying mixture specified by Frazer, Stewart, and Schulman was used. Coppock and Cookson suggest therefore that mineral oil may be safely used in making bread if it is not less pure than *B.P.* liquid paraffin and if the final proportion does not exceed 0·2%.

We know little about the effects of long-continued ingestion of mineral oils of uncertain purity; the digestion experiments quoted were artificial and may not have reproduced conditions in the alimentary tract. Moreover, prosecutions in Manchester and elsewhere have shown with painful clarity that some people will not hesitate to supply bakers with what is nothing more or less than crude motor-oil. For these reasons we agree that the use of mineral oils in foods is to be unreservedly condemned.

Influenza

There were 360 deaths in the great towns of England and Wales during the week ended March 19, compared with 321 in the previous week. There were small increases in the West Riding towns, but the principal increases were in the Midlands; for example, Birmingham had 37 deaths against 20 in the previous week. Greater London registered a small decrease from 83 to 71.

Cooling of Ice-cream

After May 1 it will be necessary for the requisite cooling apparatus to be installed in all premises where ice-cream is manufactured other than from a complete cold mix. Ice-cream manufacturers will no longer be able to plead the special defence that they have ordered but been unable to obtain the apparatus. The Minister of Health is satisfied that sufficient cooling apparatus is now on the market to satisfy all demands.

The special defence was introduced in the Ice Cream (Heat Treatment, &c.) Regulations, 1947, because at that time there was a serious shortage of cooling apparatus. It was later extended until May 1, 1949, by the Ice Cream (Heat Treatment, &c.) Amendment Regulations, 1948, made jointly by the Minister of Health and Minister of Food.

4. Stryker, W. A. *Arch. Path.* 1941, **31**, 670.
5. Frazer, A. C., Stewart, H. C., Schulman, J. H. *Nature, Lond.* 1942, **149**, 167.
6. Javert, C. T., Macri, C. *Amer. J. Obstet. Gynec.* 1941, **42**, 409.
7. *J. Amer. med. Ass.* 1947, **135**, 512.
8. *Brit. med. J.* 1948, i, 1141.
9. Coppock, J. B. M., Cookson, M. A. *Ibid*, 1949, i, 73.

Parliament

QUESTION TIME

Analgesia in Childbirth

Mrs. AYRTON GOULD asked the Minister of Health how many local authorities were providing analgesia treatment in childbirth; and to what extent he was impressing upon those who were not doing so their obligation to implement the proposals relating to analgesia approved by him under part III of the National Health Service Act.—Mr. BEVAN replied: Analgesia is being used in the domiciliary midwifery service of 134 county and county-borough councils. Individual action is being taken with the councils and county boroughs in which it is not yet being provided.

Lady TWEEDSMUIR asked the Minister if he would give the proportion of women receiving analgesia in childbirth in their own homes to the total births for the years 1947 and 1948 in England and Wales.—Mr. BEVAN replied: The following is the information asked for:

Year	Number of domiciliary confinements of which midwives were in charge	Number of domiciliary confinements where gas-and-air analgesia was administered by midwives	Percentage of col. (3) to col. (2)
(1)	(2)	(3)	(4)
1938	289,035	1,175	0·4
1939	285,024	1,029	0·4
1940	284,227	1,545	0·5
1941	268,905	1,783	0·7
1942	274,148	1,743	0·6
1943	269,579	5,207	1·2
1944	281,769	5,102	1·8
1945	245,237	7,262	3·0
1946	298,019	20,507	6·9
1947	327,245	43,683	13·3
1948	Information not yet available.		

In addition to the domiciliary confinements where a midwife is in charge there are a large number of domiciliary confinements where a doctor is in charge. These confinements numbered 95,545 in 1946 and 96,937 in 1947. Although figures are not available, it is known that analgesia or anæsthesia is given in a high proportion of these doctors' cases.

Doctors' Lists

Mr. A. C. BOSSOM asked the Minister what was the maximum number of patients he allowed a doctor to take on his panel.—Mr. BEVAN replied: 4000. Mr. BOSSOM: How long does that permit the doctor to give to each patient in considering their complaints?—Mr. BEVAN: Action is already being taken to reduce the number where it is above 4000 to that figure, but it must also be borne in mind that these are not patients, but persons on doctors' lists. I am glad that they do not all require attention at the same time.

Renewal of Prescriptions and Certificates

Mr. J. E. HAIRE asked the Minister if he would issue a circular to local medical authorities indicating that he was prepared to allow responsible persons acting for doctors to renew prescriptions and issue medical certificates.—Mr. BEVAN replied: The terms of service of general practitioners prescribe conditions subject to which qualified deputies and assistants may act for practitioners in these matters. I do not think that it would be in the public interest to extend these arrangements to unqualified persons.

Press and Hospital Management Committees

Mr. GORONWY ROBERTS asked the Minister if he would direct that the Press be admitted to meetings of hospital management committees.—Mr. BEVAN replied: I think this would be undesirable.

Digitized by Google

Analgesia in Scotland

Colonel ALAN GOMME-DUNCAN asked the Secretary of State for Scotland in how many cases in Scotland was analgesia administered by domiciliary midwives or nurses trained in midwifery in the years 1938, 1944, 1947, and 1948 respectively.—Mr. ARTHUR WOODBURN replied: There could not have been any cases in 1938 and 1944 because it was only in July, 1946, that the Central Midwives Board for Scotland authorised the administration of analgesia by midwives. In 1947 there were 120 cases and in 1948, according to preliminary returns, about 800.

Replying to further questions Mr. WOODBURN said that in Scotland more than half the cases of births outside hospitals were treated with a doctor present, and in every case the doctor had the authority over the case. Training in analgesia was now being given to certified midwives at the rate of almost 250 a year, and to all student midwives numbering about 600 a year. He hoped that by the end of 1950 over three-quarters of the midwives then practising in Scotland would have had this training, and his aim was to have the process complete by the end of 1951.

Care of the Aged in Glasgow

Mr. JAMES CARMICHAEL asked the Secretary of State for Scotland the number of aged infirm in Glasgow awaiting admission to hospital for treatment and care and the average weekly admission; and what system was adopted by the regional hospital board to see that each hospital accepted its responsibility in this essential service to the aged infirm.—Mr. WOODBURN replied: The regional hospital board are at present inquiring into this whole problem in order to determine the responsibilities of each of the hospitals concerned for this class of patient, but no complete information is yet available. The board have a central admission bureau which is gradually assuming responsibility for hospital admissions in the Glasgow area and especially for this class of person. Mr. CARMICHAEL: Surely while the inquiry is being made these aged infirm people should be entitled to some easing of their troubles?—Mr. WOODBURN: The point is that until July, 1948, the voluntary hospitals had no responsibility at all for this type of patient; that was dealt with by the local authority. This is an entirely new responsibility. Unfortunately, however, a number of people are contracting tuberculosis because there are not enough nurses to permit of hospital treatment. Therefore, in deciding who shall go into hospital first, we must select the most urgent cases. I think that many old people would agree that those whose lives are at stake should receive priority in treatment.

Milk Substitutes

Mr. BAKER WHITE asked the Lord President of the Council if he would make a statement on the results of the experiments being carried out under his auspices at Cambridge University, designed to produce milk from wheat.—Mr. HERBERT MORRISON replied: No such experiments have been carried out at Cambridge, but I believe that the question refers to observations recently made in Germany by workers for the Medical Research Council who are based on Cambridge. They have shown that a mixture including soya flour, wheat, and other cereals, to which only a small proportion of dried milk is added, promises to be a useful substitute for dried milk itself in the nutrition of children. This, of course, is a very different thing from producing milk from wheat.

Coalminers and Epidermophytosis

Mr. RONALD WILLIAMS asked the Minister of National Insurance whether he would consider adding to the list of prescribed industrial diseases epidermophytosis where that disease had been contracted by coalminers in pit-head baths.—Mr. JAMES GRIFFITHS replied: I am considering the position in relation to benefit under the Industrial Injuries Act in the light of a recent decision of the commissioner. In this case, while stating that the disease is not prescribed under the Act, he suggested that in certain circumstances it might be regarded as contracted by accident and as such already within the scope of the Act.

Dr. BARNETT STROSS: Is the Minister aware that these cases are quite numerous, tend to spread, and that they are easily preventable? Would he use this influence with the National Coal Board to see that the necessary steps are taken at the pit-head baths to ensure that further contagion is prevented?—Mr. GRIFFITHS: We have no evidence so far of any material increase in the number of cases, but I understand that they can in the ordinary way be prevented. I shall take what steps I can in association with the Minister of Fuel and Power to see what improvements can be made.

Purchase-tax on Drugs

Mr. NIALL MACPHERSON asked the Chancellor of the Exchequer whether his attention had been called to the fact that under notice 78N. issued by the Commissioners of Customs and Excise it was only permitted, in respect of certain medicines and drugs sold in multiple packs, for the outer container to bear the brand name or trade mark, and that the inner container must not bear such name or trade mark; what was the reason for this provision, and whether, in view of the special arrangements required, he would consider dispensing with it.—Mr. DOUGLAS JAY replied: The scheme explained in this notice will enable branded or proprietary forms of certain drugs and medicines to be supplied free of purchase-tax to pharmacists who require them for dispensing. Except in the case of those substances which can be supplied to the public only on a doctor's prescription, the scheme requires that the dispensed medicine shall not reach the consumer in the branded or proprietary get-up. The particular provision referred to enables perishable substances which must be dispensed in their original containers to participate in the scheme and is an essential part of it.

Mr. A. R. BLACKBURN asked the Chancellor if he was aware of the confusion caused to all concerned in the pharmaceutical industry by the accumulative and restrictive provisions of part II of the eighth schedule to the Finance Act, 1948; the Purchase Tax (No. 5) Order, 1948, S.I. 2462, the Purchase Tax (No. 6) Order, S.I. 2720, and the Purchase Tax (No. 1) Order, 1949, S.I. 46; and what steps he proposed to take to alleviate the position in the near future.—Mr. JAY replied: These provisions are intended to widen the scope of the tax exemptions for medicines in accordance with the wishes expressed on both sides of the House. When they are fully operative, their combined effect will be to exempt from tax most medicines supplied on a medical prescription, and to make available to the public tax-free a wide range of proprietary and unbranded remedies suitable for practically every complaint. The reliefs were worked out in collaboration with the trade associations of the pharmaceutical industry, and I have no reason to suppose that they will be unduly onerous in operation. Having regard to the requirements of the revenue, the alternative to the reliefs would be the reimposition of tax on all medicines, a step which I should not like to propose.

Oral Vaccines

Mr. F. J. ERROLL asked the Chancellor whether he was aware that under head IV of the Purchase Tax (No. 5) Order, 1948, vaccines had been exempted from purchase-tax so long as they were prepared for use by injection or by application to the scarified skin of the user, but that vaccines were chargeable with purchase-tax if intended for oral administration; and whether, in view of the fact that there was a growing body of favourable opinion towards the latter form of therapy, steps could be taken to ensure that vaccines for oral administration were placed in the same position as other vaccines so far as purchase-tax was concerned.—Mr. JAY replied: The trade organisation most concerned has already been informed that vaccines for oral administration will be considered when the next Treasury exemptions order is being prepared.

Female Circumcision in the Sudan

Sir BASIL NEVEN-SPENCE asked the Secretary of State for Foreign Affairs what powers he had to take proceedings against a medical practitioner, registered in the United Kingdom, who performed an operation which was illegal in the Sudan.—Mr. C. P. MAYHEW: I am advised that a registered medical practitioner may be summoned to appear before the General Medical Council if he performs in the Sudan an operation which is illegal there, and if found guilty may have his name erased from the Medical Register. Further, any person who performs in the Sudan an operation which is illegal there, can, while in the Sudan, be prosecuted under the Sudan Criminal Code.

Sir BASIL NEVEN-SPENCE: Does the converse hold true? If, for example, the Sudanese government were to legalise the operation of female circumcision as practised in Egypt, which would be acceptable to the Sudanese, would any medical practitioner doing the operation, supervising it, or allowing it to be done in his hospital be liable to be hauled before the General Medical Council?—Mr. MAYHEW: Yes, Sir, I understand that is so.

Digitized by Google

Obituary

WILLIAM JOHNSON

M.C., M.D. LOND, F.R.C.P.

Dr. William Johnson, consulting physician to the Royal Liverpool United Hospital, who died on March 15 at the age of 63, was a Guy's student, and the influence of Arthur Hurst coloured much of his medical career. After qualifying in 1908 he became Hurst's first house-physician. Later, with a Gull research studentship in pathology, he worked under A. E. Boycott.

In the war of 1914–18 he served in France with the R.A.M.C. and won the Military Cross. Working under Dr. Gordon Holmes at no. 62 casualty-clearing station, he gained an exceptional experience in the psychoneuroses of war, and he afterwards contributed the account of Neuroses in France to the *Official Medical History of the War*. When he was demobilised he worked with Hurst's neurological cases at Guy's, while Hurst was still at Seale Hayne in Devon. But no further opening offered itself, and Johnson, whose parents lived at Wrexham, returned to the North as assistant physician to the Royal Southern Hospital and the Children's Hospital at Liverpool.

Though his special interests were neurological, he was never an exclusive specialist, and he remained one of the lessening band of general physicians, at home in all aspects of medicine, and with wide practical interests. He did much, for example, to establish and sustain the magnificent physiotherapy school attached to "the Southern." As consulting physician to the Ministry of Pensions Hospital at Mossley Hill, he retained his keen interest in the medical casualties of war. He was a faithful and devoted teacher of nurses, and always thought the education of the nurse as important as that of the medical student. He had also a large experience of the law-courts, and his opinion was much sought; as a witness, he was dignified and quietly impressive, and he was regarded by our legal colleagues as a man of scrupulous fairness and honesty. Recently, he had been appointed by the Ministry of National Insurance as a member of the Medical Appeal Tribunal in Liverpool under the new Act. For many years, he was visiting physician to the Birkenhead Municipal Hospital, and over the last decade or two he had made a patient and friendly contribution towards the raising of medical standards in local-authority hospitals. He was a conscientious committee man, and after his retirement from the active staff of his hospital, he was asked to become chairman of several important local committees under the National Health Service Act.

In his later years, it seemed natural that he should be called to positions which showed what his colleagues thought of him—president of the Liverpool Medical Institution, chairman of the medical faculty of the university, president of the section of neurology of the Royal Society of Medicine, examiner for the Conjoint board and various universities, and censor of the Royal College of Physicians, to whose fellowship he had been elected in 1926.

"Johnson," writes R. C., "was one of those solid, wholly dependable characters of whom it could be said that 'they maintain the fabric of the world, and in the handiwork of their craft is their prayer.' As a physician, he was shrewd, wise, and beloved by his patients, and by the nurses, who in his later years referred affectionately to him as Daddy. With his students he was popular, and the family of students and housemen which he fathered through the years will think of him with affection and gratitude for what he taught them. I doubt if he had a single enemy. He was a kind man, equable and rarely ruffled; but, though apparently easy-going, he could be surprisingly obstinate and uncompromising on some matter which engaged his loyalty or his conviction. It is doubtful if he ever said anything unkind about his colleagues, lay or medical, however irritating they might be; on the other hand, he often found excuses for their behaviour. On the surface, he might appear serious; underneath there was a delight in friendly contacts, good humour, a love of good literature, and a serene happiness among his family. A few years ago, he moved out of Liverpool into the country and became a keen gardener. It was in keeping that the last farewell to him was in the sunshine of a lovely spring day, in a country churchyard. There are those of whom it is more natural to say, 'I am glad that he lived,' rather than 'I am sorry that he died.' Will Johnson was such a one."

He leaves a widow, a son, and three daughters. One of his daughters is a house-physician at his old hospital.

THOMAS MORRISON CLAYTON

M.D., D.HY. DURH., F.R.S.E.

Dr. T. Morrison Clayton, who died on March 21, had a long and distinguished career as medical officer of health for Gateshead. Born at Felling in 1870, he graduated from the University of Durham in 1894 and practised in his native town for some years, becoming its M.O.H. in 1896. Six years later he succeeded Dr. R. Greene as the fourth whole-time medical officer of Gateshead, a town which shared the unenviable reputation of industrial Tyneside as an unhealthy area. He belonged to the generation for which preventive medicine was mainly concerned with environment and the infectious diseases, and he became an expert epidemiologist: he dealt with the last local outbreaks of typhus, in 1907 and 1910. He also initiated school medical inspection in Gateshead in 1907, and organised the maternity and child-welfare service in 1919. Throughout his service he was medical superintendent of Sheriff Hill Isolation Hospital, and he started the extension of the Gateshead municipal hospitals by the opening of Whinney House Sanatorium in 1925. But in hospital development he was gravely handicapped by the poverty of the town, which became a distressed area in the post-war slump. He retired in 1936 before grants from the Special Areas Commissioner made possible the erection of the new municipal hospitals which were the logical fruition of much of his work.

J. G. writes: "Exceptionally well qualified, Clayton was an authority on the infectious diseases, and his opinion was sought and valued by his colleagues. One of the first to criticise the theory of the aerial convection of smallpox, he ascribed the apparent examples of such spread rather to human contact, a thesis which he developed in 1905 before the leading sanitarians of the country. An excellent raconteur, he had the happy knack of smoothing out many administrative and other difficulties with a well-timed and pointed anecdote."

Dr. Clayton is survived by two daughters and three sons, two of whom are medical officers of health.

JOHN WEIR WEST

C.B., C.M.G., C.B.E., M.CH. R.U.I., LL.D. BELF.

Major-General West, formerly consulting surgeon to the Army and professor of military surgery at the Royal Army Medical College, Millbank, died at Fleet, in Hampshire, on March 6. He was born in 1875, the son of the Rev. T. West, who was at one time moderator of the Irish Presbyterian Church. From the Royal Academical Institution in Belfast he went on to the Queen's College where he graduated M.B. in 1899. The following year he joined the R.A.M.C., and in 1901 he proceeded to South Africa where he took part in operations in Cape Colony and the Orange River Colony. In 1914 he was sent to France with the original Expeditionary Force in charge of the 3rd cavalry field ambulance. Later he commanded the 62nd general hospital in Italy. A chevalier of the Legion of Honour, he also received the Italian order della Salute Publico, and in 1919 he was appointed C.M.G. During these arduous years he had found time in 1917 to take his M.CH., and in 1924 he became consulting surgeon to the Army, an appointment he held till in 1927 he was posted to the Burma district

Digitized by Google

as A.D.M.S. Here he once more saw active service, and he was mentioned in despatches and appointed C.B.E. in 1932 after his return to this country. For the next three years he held the chair in military surgery at Millbank and again acted as consulting surgeon to the Army. After his retirement in 1935 he spent four years as superintendent of the convalescent home for officers in the Isle of Wight, and during the late war he was deputy superintendent of Botleys Park War Hospital. From 1942 to 1945 he was colonel commandant of the R.A.M.C.

"The name of Johnnie West," writes J. A. H., "will always be associated with military surgery, which he did so much to foster. An excellent surgeon himself, he was always on the look-out for promise among his junior officers, and to give them every opportunity to develop their talent. He was an indefatigable worker, always ready to answer a call for advice or help, and his routine visits to hospitals were looked forward to by medical officers, nursing sisters, and orderlies alike. For the British soldier, whose confidence he won to an unusual degree, he had a great affection. The happy relationship which has existed between military surgeons and their civilian colleagues for many years is largely due to his influence. As consulting surgeon he was adviser to the several director-generals under whom he served in all matters directly or indirectly connected with military surgery in peace and in preparation for war, and I remember with gratitude how invaluable his counsel was. Always cheery and good-tempered, his two main characteristics were a very high sense of duty and a deep affection for his corps. No officer of my time served it with more single-minded devotion."

General West married in 1905 Dora Isabel, daughter of Surgeon Major Andrew Rickards. She survives him with one daughter.

JOHN RICHARD TARRANT CONNER

M.D. R.U.I.

Dr. J. R. Conner, editor of the *Medical Review* for more than 30 years, was a graduate in arts and medicine—in both of which he took honours—of Queen's College, Cork. He completed his medical studies at St. Thomas's Hospital.

After qualifying in 1886 he early began to devote his time to medical journalism, and his work as a man of letters covers more than half a century. He was a contributor to the *Medical Review* some 50 years ago, and when its founder retired, he assumed sole responsibility. The 1914–18 war brought this journal to an end, but the reputation Conner enjoyed in the publishing world gave him the editorship of the *Hospital*, and later of the *Clinical Journal*. This work and his regular letters as London correspondent of the *Journal of the American Medical Association* he continued till his death. In his earlier years he was also a frequent contributor to our columns.

"For several decades," writes a colleague, "the *Medical Review* embodied Conner's ideas of what a medical journal should be. An omnivorous reader, with a critical attitude towards abstractions—he used to say that a characteristic feature of the English was a love of the concrete—he combed the world's medical press for whatever seemed of real value and put it into the journal. It was a labour of love which gave him infinite satisfaction but no great wealth. To his juniors in letters he was prodigal in his generosity, taking infinite pains to show them the tricks of their trade. Economy of words and clarity of expression were some of the lessons he taught when he returned a typescript heavily blue-pencilled. His close association with Sir Jonathan Hutchinson did much to foster his taste for critical observation and dispassionate judgment, and he was unswerving in his ambition to be impartial in his reporting of medical events. In his editorial capacity he corresponded at some time or other with nearly all the leading medical authorities in Great Britain. But though he knew much about them, they knew little or nothing about him, meeting him seldom or never, and he was content to remain behind the scenes. His was a happy old age, partly because his work kept him in harness all the time, partly because his devotion to his wife and his pride in his son made life warm and rich for him till the end."

Shortly before his death, Dr. Conner and his wife moved from the house in which they had lived for so long in the North of London to make their home with their only son, the Vicar of All Hallows at Greenford. He died there on March 16 at the age of 87.

GEORGE MORRIS STOKER

M.R.C.S.

Dr. Stoker, who died on March 21 at Guy's Hospital after a short illness, was 50 years of age. Educated at Dover College, he served in the first world war with a commission in the Royal Field Artillery. He completed his training in medicine at Guy's in 1922, and settled in practice at Mitcham in Surrey 25 years ago. From the inception of the Wilson Hospital, Mitcham, in 1928, he took an active part in everything connected with it: during the late war he was its medical superintendent and lived in the hospital—except for the few months following D-day, when he was transferred to Botleys Park Hospital. His interest was surgery, and besides running a large general practice he held appointments as ear, nose, and throat surgeon at St. George's Dispensary for Children, Blackfriars Road, and as consultant for the enuresis clinic at All Saints' Hospital, in addition to his appointment as surgeon to the Wilson Hospital. For many years he was a member of the council of the Medical Protection Society, and in 1948 he was appointed chairman of the council—a post which he filled with his usual competence, common sense, and good humour. He was also a member of the Surrey local medical committee, and, more recently, of the medical committee of the St. Helier group hospitals. His other great interest lay in the St. John Ambulance Brigade, which he joined as a divisional surgeon in 1928, being promoted to county surgeon in 1930, and assistant commissioner (southern area) in 1947. In 1942 he was made a serving brother of the Order of St. John. In the district he served so well and in so many ways his early death will be deeply regretted.

Watt & Sons

Dr. Stoker leaves a widow, and two sons, one of whom is in his fourth year at Guy's Hospital.

Diary of the Week

APRIL 3 TO 9

Tuesday, 5th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. A. P. Thomson: Problems of Ageing and Chronic Sickness. (First Lumleian lecture.)

Wednesday, 6th

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5.30 P.M. Dr. Erik Lindgren (Stockholm): Present Day Neuroradiology.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
NOON. Mr. J. D. McLaggan: The Larynx.

HARVEIAN SOCIETY OF LONDON
8.15 P.M. (26, Portland Place, W.1.) Dr. Russell Reynolds: Ciné-radiography.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. L. G. Housden: The Growing Family under Modern Home Conditions.

Thursday, 7th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Thomson: Problems of Ageing and Chronic Sickness. (Last Lumleian lecture.)

ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. *Medical group.* Mr. J. F. V. Larway: Group Hospital Medical Photography.

Friday, 8th

UNIVERSITY OF LONDON
5.30 P.M. (London School of Hygiene, Keppel Street, W.C.1.) Prof. J. H. Biggart: Hypersensitivity in Disease.

EMPIRE RHEUMATISM COUNCIL
4.30 P.M. (Apothecaries' Hall, Black Friars Lane, E.C.4.) Sir Adolphe Abrahams: Rheumatism—a Symptom in Clinical Diagnosis. (Opening lecture of spring weekend course.)

Digitized by Google

Notes and News

PATTERN OF OUR HEALTH SERVICES

Dr. J. B. Grant, director for Europe of the international health division of the Rockefeller Foundation, sketched for the Institute of Almoners, at their annual general meeting on March 25, his idea of the pattern which health services will take in the future. Koch and Pasteur, he suggested, had in some ways retarded medical development by 50 years, and we were only now lifting our eyes from an overclose study of the minutiæ of clinical pathology to look at the over-all picture which included social physiology, social pathology, and social therapy.

The background of all health services was social legislation, which had made enormous strides in this century. He could himself remember when family allowances, for instance, were termed "rank communism"; yet today they were included in the legislative programme of 30 countries. In the future, as he saw it, economic barriers to medical care would be removed by taxation and insurance. But an efficient health service would depend on the provision of efficient and well-trained personnel and adequate equipment. He believed that proper distribution would be achieved by grouping the service in regions, based on a teaching hospital and stretching through several levels to the community health centre on the periphery. There should be a two-way flow of patients from the health centre to the teaching hospital, and the quality of the service, he held, would be determined by the standards maintained at the periphery rather than at the base.

The Dawson report of 1920 would, Dr. Grant declared, be document no. 1 in planning health services all over the world, and he was reproachful that, in the country where the report had been written, health centres should still, nearly 30 years later, be "way round the horizon." The work of the centres would be based on the unit of the family and not the individual, and it would be carried out by a team of workers captained by the general practitioner. If the doctor was to practise social medicine he must have facilities for obtaining the social history of his patients, and much would depend on his aptitude for making full use of his team of case-workers and other ancillaries.

ANALGESIA IN CHILDBIRTH IN LONDON

DURING the past week London County Council midwives attended 156 confinements and in 113, that is 72%, analgesia was used. For the 43 who did not have it, the reasons were:

21 owing to the time factor—e.g., born before arrival of midwife, rapid labour; 7 had no medical certificate of fitness for analgesia; 3 were medically unfit—e.g., bronchitis; 6 refused to have it; 3 maternity nursing cases (the doctor is responsible for these cases and probably gave an anæsthetic); 3 other reasons (stillbirths, abortions).

All the full-time midwives employed by the council are trained in its use (except one who is being trained). The apparatus is kept at the accident ambulance stations and is ordered by the midwife when she needs it It is delivered by an accident ambulance to the home within a few minutes. The Council also has agreements for domiciliary midwifery with hospitals and district-nursing associations; all their midwives are trained to give analgesia.

THE BELSEN TRIAL

IN April, 1945, British officers entered the notorious concentration camp at Belsen and found some 40,000 men and women confined in an area approximately 1500 by 350 metres. All were starved. Many suffered from typhus. There were 13,000 unburied corpses, scarcely any sleeping accommodation, and no medical assistance. After careful inquiries Josef Kramer, the commandant, and over 40 others were put upon their trial. An account of the proceedings, admirably edited by Mr. Raymond Phillips, is now published in the War Crimes Trials series.[1] It was the first trial held under international law. The accused were charged with "committing war crimes" in that they, between named dates, being members of the camp staffs responsible for the well-being of the Allied nationals interned, "in violation of the Law and Usages of War" were together concerned in ill-treating the internees and causing their death and physical suffering. The charges related not only to Belsen but also to the extermination camp at Auschwitz where thousands were dispatched to gas chambers and crematoria. Some of the accused had been both at Belsen and Auschwitz, others at one camp only. One accused, Dr. Fritz Klein, had been the camp doctor. There was little proof that he had personally ill-treated anyone, but he had selected victims for the gas chamber without protest. The accused were defended by twelve officers, almost all British and all members of the legal profession in civil life. Their main defence was obedience to superior orders—a plea which the *Manual of Military Law* did not very definitely reject until it was amended in April, 1944. Kramer, Klein, and 9 others were sentenced to death, and 19 more to imprisonment; 14 others were acquitted.

The procedure was governed by the Regulations for Trial of War Criminals, issued under royal warrant in 1945. These applied the rules prescribed for field general courts martial, but admitted evidence by affidavit which involved the never quite satisfactory element of photographic identification. The number of the accused and the need of interpreters' services may account for the length of the trial—54 days. The Lord Chancellor, in a foreword to the book, praises the fairness of court-martial trial for Service offences, but suggests that an experienced judge, sitting with assessors, would have disposed of the cases more quickly.

Even apart from the evidence of cannibalism among the starving prisoners, and the references to scientific or pseudo-scientific experiments upon unwilling human guineapigs, the story and the photographs published in this book are a record of almost indescribable horrors. We may join with Lord Jowitt in the hope that the facts here revealed will make it unnecessary that any similar trial should ever be conducted again.

1. The Belsen Trial (War Crimes Trials Vol. II). Editor: RAYMOND PHILLIPS, M.C., B.C.L., barrister-at-law, with a foreword by Lord Jowitt. London: Wm. Hodge. 1949. Pp. 749. 30s.

SCORPION STINGS

IN the last twelve years [1] the Institut Pasteur of Algeria has received 4057 medical reports of the results of treating with its serum victims of scorpion stings. The patient's life was considered by the doctor to be endangered in 1003 of them, of whom 923 (92%) were saved. There are in Algeria seven species, belonging to four genera, of scorpions, but serum prepared with the venom of one of these (*Prionurus australis*) is equally potent against the venom of all of them. An interesting fact is that one of the species (*Buthus occitanus*) produces lethal venom when it is a native of northern Africa but not when it is a native of southern Europe.

WHITAKER

IN a legend wreathed about by zodiacal and agricultural symbols *Whitaker's Almanack for 1949* [2] declares itself to contain "an account of the Astronomical and other Phenomena and a vast Amount of Information respecting the Government, Finances, Population, Commerce, and General Statistics of the various Nations of the World with an Index containing 35,000 References." This should be enough for anybody, but we particularly commend to our contributors the neat article on proof-correction on p. 1032. No educated home is furnished without Whitaker, as an early advertisement might have said.

RELEASE OF DOCTORS FROM SERVICES

THE Central Medical War Committee have been informed that the release of medical officers during the coming months will be as follows:

Royal Navy.—Groups 101 and 102, April; groups 103 and 104, May; groups 105 and 106, June.
R.A.M.C.—Group 106, April 1–14; group 107, April 15–28; group 108, April 29–May 13; group 109, May 14–28; group 110; May 29–June 12; group 111, June 13–27: group 112, starting on June 28.
R.A.F.—Groups 101 and 102, April.

University of Cambridge

St. John's College.—Mr. Geoffrey Keynes will deliver the Linacre lecture at the anatomy school on Friday, May 6, at 5 P.M. He is to speak on the Personality of William Harvey.

University of Dublin

At a recent examination for the D.G.O. held at the school of physic, Trinity College, the following were successful:

Adly Aziz, Umeschandra Bardolai, Harpal Kaur Brar, Nilkanth Mahadeo Damle, Dhireshwar Shankardas Desai, W. G. Dixon, Herman Kessel, M. W. Livingston, Ahmed Mansi, Aminah Sabri Murad, Zubaida Nasiruddin, Wadea Fathulla Rassam, Iskander Masoud Shenouda, Sarah T. Thomas.

1. Sergent, E. *Ann. Inst. Pasteur*, 1949, 76, 50.
2. London: 13, Bedford Square, W.C.1. Pp. 1126. 12s. 6d.

Digitized by Google

Society of Apothecaries of London

The court of assistants met recently under the chairmanship of Prof. E. C. Dodds, F.R.S., master of the society. Dr. J. P. Hedley was reappointed to represent the society on the Central Midwives Board.

The society's gold medal for 1949 is to be bestowed upon Prof. Jacques Tréfouël, director of the Institut Pasteur, Paris, in commemoration of his contribution to therapeutics. It was resolved to confer the honorary freedom of the society upon Sir Charles Harington, F.R.S., in recognition of his work in biochemistry and chemical pathology.

The Gillson scholarship in pathology will in future be awarded every third year, beginning in 1952, in the sum of £500.

The following were clothed with the livery of the society:

J. F. Wilkinson, H. C. Edwards, A. G. S. Bailey, Alexander Cowan, A. J. M. Reese, F. N. Reynolds.

The following were admitted to the freedom of the society:

By redemption, G. E. Parker, Arthur Willcox, A. C. F. Green, E. R. Cullinan, A. C. Thackray, F. A. Greene, Bruce Maclean, A. L. Walker, D. Evan Bedford, C. G. Roberts, E. W. Riches, D. F. Little, J. F. Wilkinson, R. T. T. Warwick, J. A. Gorsky; by gift, L. T. Moore (consulting architect to the society); by servitude, G. J. Hamilton, P. R. Dearman; by patrimony, J. F. Fisher, Enid Houghton.

The following diplomas were granted upon examination:

Mastery of Midwifery.—G. Bridge.

Industrial Health.—N. Graham, J. G. Jones, G. MacBain, T. E. M. Wardill.

L.M.S.S.A.—H. H. B. Perkins, C. M. D. Davies, M. A. R. Stilson, H. D. Isaacs, A. Paes, M. J. Beilin, J. A. A. R. Venniker, E. G. Dimopoulos, M. Caller, J. K. Jones, M. G. Kaye, T. Bell, J. R. Deacon, D. L. Stilson, J. D. Whittall, T. Brearley, J. R. Dyson, T. Pimblett, C. Jones, R. W. E. Brain, R. Raynham, N. H. Porter, R. F. Maddox, D. L. Stewart, A. P. Caspers, R. Payne, G. Williams, H. G. Damant, B. E. L. Thompson, N. H. Bamford, E. F. Stafford, M. H. Symes, E. A. Brown.

Brompton Hospital Dinner

A dinner for the medical staff and former residents will be held in London in November to mark the centenary of the hospital. Further particulars will be found in our advertisement columns.

Naval Medical Compassionate Fund

A meeting of the subscribers to the fund will be held at 3 P.M. on April 22 at the medical department of the Navy, Queen Anne's Mansions, St. James's Park, London, S.W.1, to elect six directors.

Blood Donors

Over 380,000 blood donations were received by the National Blood Transfusion Service last year. This was 90,000 more than 1947; but more blood was used last year in hospitals in England and Wales than in 1944, the peak year of the war. During the year nearly 100,000 new donors joined the National Blood Transfusion Service, making a total of 373,778. But to provide for future needs and to reduce calls on existing donors, another 200,000 are wanted.

International Congress on Obstetrics and Gynæcology

This congress, which is sponsored by the American Committee on Maternal Welfare, will be held from May 14 to 19, 1950, at Hotel Statler, New York. The scientific sessions will include discussions on the physiology and pathology of human reproduction, social and economic problems, neoplastic diseases of the female reproductive system, and obstetric and gynæcological procedures. Further information may be had from Dr. Fred L. Adair, 24, West Ohio Street, Chicago 10, Illinois.

Council for Coördination of Medical Science Congresses

UNESCO and W.H.O. are sponsoring a conference, which will open in Brussels on April 4, to discuss the establishment of this council. Since last April an organising committee, headed by Prof. J. Maisin have been considering what the functions of the new council should be. At the Brussels conference they will propose that it should

collect information on all international and national organisations of a medical or related character and on their congresses

suggest appropriate dates and plans for the holding of congresses and in particular for the grouping of disciplines

give financial assistance to the scientific work of congresses

provide assistance to enable certain members to attend the congresses

organise specialised courses during or in connexion with congresses for the benefit of physicians

study the problem of dissemination of scientific material resulting rom congresses.

Royal Society of Edinburgh

Those elected to the fellowship on March 7 included: Dr. D. P. Cuthbertson, Dr. A. M. Gillespie, Dr. Harold Sington, and Dr. R. H. A. Swain.

British Orthopædic Association

The spring meeting of the association will be held at the University of Nottingham on April 22 and 23 under the presidency of Mr. S. A. S. Malkin.

Prof. Alexander Haddow is visiting Italy, under the auspices of the British Council, to lecture on the chemotherapy of cancer.

The *Report of the Water Pollution Research Board for the Year 1947* has been published for the Department of Scientific and Industrial Research by H.M. Stationery Office, from which the report is obtainable, price 1*s.* 6*d.*

The wall chart of identification colours for gas cylinders published by the British Standards Institution in 1932, has been amended and reissued. Copies may be had from the sales department of the institution, 24, Victoria Street, London, S.W.1, at the following prices: 10*s.* 6*d.* mounted, 6*s.* 6*d.* unmounted.

CORRIGENDUM.—*Action of Dihydroergocornine on the Circulation.*—In this article by Professor Goetz, published in our last issue, the sentence beginning 22 lines from the end of the second column on p. 510 should read: "Of the hypertensives, 16 were retested after they had undergone subtotal sympathectomy (removal of the splanchnic nerves and the sympathetic chain from $D_{3(2)}$ to L_2)."

Births, Marriages, and Deaths

BIRTHS

BROWN.—On March 23, in London, the wife of Dr. P. E. Brown—a daughter.

CHASE.—On March 23, at West Kirby, the wife of Dr. W. H. Chase—a son.

DISMORR.—On March 22, at Birchington, the wife of Dr. P. C. Dismorr—a daughter.

FIGGIS.—On March 22, in London, the wife of Dr. Morton Figgis—a daughter.

HARLAND.—On March 18, in London, the wife of Dr. J. C. Harland—a son.

HAYWARD.—On March 24, in London, the wife of Dr. G. W. Hayward—a daughter.

MCSHEEHY.—On March 22, at Aldershot, the wife of Major H. O. P. McSheehy, R.A.M.C.—a son.

MILLER.—On March 21, at Newcastle-on-Tyne, to Dr. Eileen Miller (*née* Baird), wife of Dr. Henry Miller—a son.

MOFFAT.—On March 19, at Castle Douglas, the wife of Dr. J. R. Moffat—a son.

PARRY.—On March 23, in London, the wife of Dr. Hugh Parry—a son.

RADFORD.—On March 21, at Bristol, the wife of Dr. Philip Radford—a daughter.

RICE.—On March 21, in London, the wife of Dr. H. M. Rice—a daughter.

RUBEN.—On March 24, in London, to Dr. Joan N. Ruben (*née* Mackover), wife of Dr. Cecil M. Ruben—a son.

SARGENT.—On March 24, in London, the wife of Dr. Frank Sargent—a daughter.

MARRIAGES

HAVELOCK—BUCK.—On March 19, at Ealing, Mr. Brian J. R. Havelock to Dr. Joyce Buck.

WADSWORTH—CHUD.—On March 26, in Singapore, George Reginald Wadsworth, M.B., to Chud Swee Liew.

DEATHS

BUDDEN—On March 25, at Dorking, Tice Fisher Budden, M.D. Camb., aged 82.

CRAIG.—On March 23, Charles Hawkins Craig, M.B. Edin., aged 78.

DAVENPORT.—On March 22, in London, Percival Arthur Clive Davenport, lieut.-colonel, I.M.S. retd.

GREEN.—On March 26, at Prescot, Lancs, Samuel Morris Green, M.R.C.S., D.P.H., aged 72.

HAMILTON.—On March 17, at Adelaide, South Australia, Charles Wolfe Hamilton, M.D.

HOPE.—On March 21, at Gosforth, Newcastle-on-Tyne, Minnie Edith Hope, M.R.C.S., D.M.R.E.

JOHNSON.—On March 19, at Oxford, Brian Ingram Johnson, B.M. Oxfd.

KENT.—On March 16, Charles Arthur Kent, M.D., B.SC. Lond., D.P.H., aged 81.

LEGGE.—On March 26, Sydney Buxton Legge, M.D. Edin.

LYNE.—On March 19, at Kew, Surrey, Charles Virgil Nunez Lyne, M.R.C.S., aged 82.

STOKER.—On March 21, in London, George Morris Stoker, M.R.C.S.

THOMAS.—On March 22, at Bournemouth, Frank Griffith Thomas, B.A., M.B. Camb., aged 76.

Digitized by Google

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

TREATMENT OF CONGESTIVE HEART-FAILURE

H. A. REID
M.B. Edin., M.R.C.P.E.
REGISTRAR

WILLIAM HUGHES
M.D. N.U.I., M.R.C.P.
SENIOR RESIDENT MEDICAL OFFICER

BELMONT ROAD HOSPITAL, LIVERPOOL

THE origin of œdema in congestive heart-failure is obscure. Until recently medical opinion was satisfied with the view that peripheral œdema derived from increased hydrostatic pressure in the capillaries, which in turn could be traced to elevated venous pressure resulting from damming up of the blood on the right side of the heart. A more recent hypothesis (Proger et al. 1942, Warren and Stead 1944, Merrill 1946, Merrill and Cargill 1947, Mokotoff and Ross 1947, Leiter 1948) would fit œdema into the mechanism of heart-failure thus: myocardial insufficiency→decreased cardiac output→decreased renal blood-flow→low glomerular filtration→low salt clearance→œdema and increased blood volume→venous hypertension.

Neither hypothesis covers all the facts (Landis et al. 1946, McMichael 1947, Burch 1947, Crutchfield and Wood 1948), but the second recognises the rôle of sodium retention in the development of the syndrome of congestive heart-failure, and provides a theoretical basis for the success of salt restriction in therapy. Restriction of salt intake as the basis of a therapeutic régime dates from the work of Karell in 1866; its importance was emphasised by Schroeder (1941), and thereafter by an increasing number of American workers (Proger et al. 1942, Schemm 1942, 1944, Wheeler et al. 1947).

Water restriction has been adversely criticised by Schemm (1942, 1944), who recommends a high fluid intake in congestive heart-failure to "wash out" the excess of extracellular sodium. His claims, however, have not been supported by other workers, most of whom advocate only as much fluid as each patient desires. Crutchfield and Wood (1948) have reviewed the literature.

During six months we have investigated some of the possible combinations of normal-sodium and low-sodium diets with varying fluid intake in the treatment of congestive heart-failure.

METHOD

Each patient was subjected to a detailed clinical examination on admission, and a clinical assessment, especially as regards œdema and hydration, was made daily. The patient was weighed on admission and thereafter at short intervals. Electrocardiography and radiography were done as soon as his condition permitted. The daily fluid intake was charted, and the output was estimated by providing the patient with a bucket under his bed in which all urine was collected and measured every 24 hours. A specimen was taken from this every morning for chloride estimation. We used the Fantus (1936) test as a routine.

In this test 10 drops of urine are introduced into a small test tube and one drop of 20% potassium bichromate is added as indicator. Silver nitrate 2·9% solution is added drop by drop until a permanent red colour develops. The number of drops added is taken as the number of grammes of chloride per litre.

The chief virtues of this ward test are speed and simplicity. It has many disadvantages—e.g., it will not measure less than 1 g. of chloride per litre. Checking results against the Volhard technique we found a reasonable correspondence. Both techniques estimate chloride, which is only a rough guide to the amount of sodium present, but in spite of its limitations and inaccuracies we found the Fantus test a most useful clinical aid in our observations.

The following "salt-free diet" was used throughout the investigation:

Breakfast
Salt-free porridge, bread or toast, margarine, jam as desired.
Salt-free fish-cake or breakfast patty.
Tea with milk and sugar as desired.

Dinner
Meat or fish (unsalted).
Potatoes (boiled, fried, or roasted), vegetable (any except baked beans, celery, parsnips, or spinach).
Stewed fruit and custard or pudding (semolina, tapioca, rice substitute, suet, blancmange).
Salt-free pastry as desired.

Tea
Salt-free bread, margarine, cake (or trifle made from salt-free cake), jam as desired.
Egg, or tripe and onions, or jelly and custard, or lettuce and tomatoes.
Tea with milk and sugar as desired.

Supper
Tea or coffee with milk and sugar as desired.
Salt-free bread and margarine if desired.

General
No salt or baking soda used in preparation and cooking.
Vinegar, mustard, and pepper as desired.
Only tea, coffee, milk, fruit juice and water permitted as drinks.
Arachis oil used for frying, &c.

With the following daily allowances (in ounces)—porridge 10, bread 9, margarine 1, jam 1, milk 12, meat 3 or fish 6, potatoes 4, vegetable 3, stewed fruit 4, cake 3, sugar 1—we have calculated from McCance and Widdowson's (1946) tables that the diet provides about 2000 calories (protein 75·6 g., fat 73·6 g., carbohydrate 267·7 g.) and less than 0·5 g. of sodium. Not all patients consume as much as this, especially in the early stages, but a diet of relatively high caloric content with a generous protein allowance was designed because many of our patients on admission suffer in addition from malnutrition.

MATERIAL

We observed 107 patients—61 males and 46 females. Of these, 64 were discharged free from œdema, and 43 died (23 of these were moribund on admission and died within 48 hours). Age-distribution, mortality, and diagnosis are summarised in the accompanying table.

CLINICAL OBSERVATIONS

Salt Restriction

Many variables must be considered in assessing a particular treatment in congestive heart-failure. Consequently it is extremely difficult to be sure that restriction of sodium intake to below 0·5 g. daily is necessary in a particular case. In 4 cases, however, there was evidence that such restriction was essential to rid the patient of œdema. In 3 of these routine treatment with digitalis and frequent mercurial diuretics did not produce any appreciable clinical improvement until the sodium intake had been restricted to less than 0·5 g. daily.

In the fourth case rest, digitalisation, and frequent mercurial diuretics led to a loss of 8·5 kg. (19 lb.) in

AGE-DISTRIBUTION, MORTALITY, AND DIAGNOSIS

Diagnosis	Age-groups									
	Recovered					Died				
	Under 50	50–59	60–69	70 and over	Total	Under 50	50–59	60–69	70 and over	Total
Coronary disease	...	2	9	18	29	..	1	5	16	22
Hypertensive disease ..	..	1	6	14	21	..	..	..	7	7
Cor pulmonale ..	..	4	3	..	7	2	2	5	2	11
Rheumatic disease ..	3	..	..	..	3	1	1	..	..	2
Other states ..	..	1	..	3	4	..	..	..	1	1
Total ..	3	8	18	35	64	3	4	10	26	43

Digitized by Google

8 days on an ordinary diet. During the next 13 days on the same régime there was no further loss of weight —in fact there was a slight gain. "Salt-free diet" was then instituted, and the mercurial diuretics were continued, but no further digitalis was given. The patient lost a further 11·5 kg. (25 lb.) and became œdema-free in 14 days (fig. 1).

When the œdema had cleared on low-sodium diet and the patients were given the ordinary hospital diet, the sequence of events varied. Some patients remained œdema-free with or without digitalis during the rest of their stay in hospital. Clinically these were the mildest cases. In the severe cases, however, reversion to ordinary diet with unlimited sodium intake led to increase of weight, return of pitting œdema, and clinical relapse. This sequence has already been illustrated by Proger et al. (1942), and we confirmed their findings in four observations, each on a different patient. The following is an example:

Case 1.—Male, aged 76. Hypertensive failure, with moderate œdema, transudate occupying lower third of right pleural cavity, blood-pressure 205/110, and auricular fibrillation.

He was digitalised and, after 4 days, put on "salt-free diet." In spite of this his œdema and weight remained stationary for the next 10 days, ventricular rate being 70–80. He was then given two injections of mersalyl 2 ml. and within a week lost 4·5 kg. (10 lb.); and his œdema, including the pleural transudate, cleared. He remained œdema-free on digitalis and "salt-free diet" for the next 2½ weeks. An ordinary diet with continuation of digitalis was then prescribed. In the next 10 days he gained 6 kg. (13 lb.) with return of œdema, dyspnœa, and right pleural transudate (presence and disappearance confirmed by X rays on each occasion). There was no change in his activity during this period.

When "salt-free diet" was again instituted, he lost 5·5 kg. (12 lb.), and his œdema cleared within 12 days. During this period he had no digitalis. Mersalyl 2 ml. was given 3 days after he went back on to the "salt-free diet" (fig. 2).

During the acute stage there were few complaints about the "salt-free diet." This may be due to the fact that many of these patients could only take drinks with very little solid food. During convalescence, complaints were more frequent; but several patients, who after discharge have continued with a low-sodium diet (so far as is practicable), say that they prefer this to the alternative of mercurial injections.

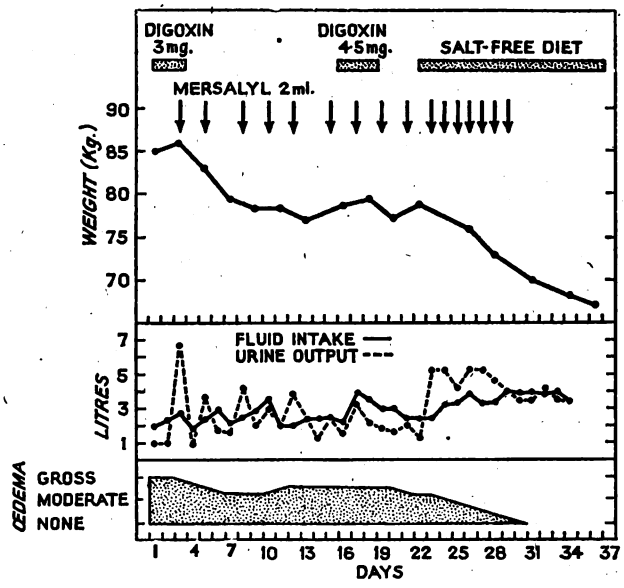


Fig. 1—Coronary disease in a male, aged 69, showing limited response to digitalis and mersalyl with unrestricted sodium intake, and complete clearance of œdema on "salt-free diet" and mersalyl without digitalis.

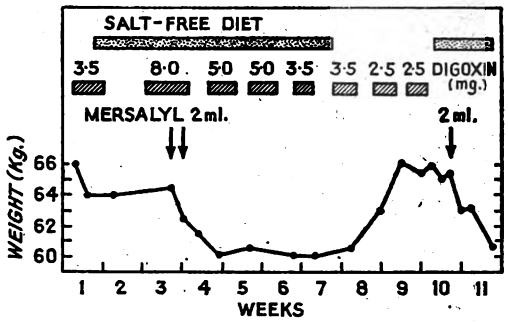


Fig. 2—Hypertensive heart-failure with auricular fibrillation (case 1), showing recurrence of congestive failure on unrestricted sodium intake despite continuation of digitalis.

High-fluid Régime

We explored the technique by taking on a case which had proved resistant to treatment with ordinary diet, digitalis, and occasional mercurial diuretics.

Case 2.—Female, aged 53. Hypertensive failure and auricular fibrillation, ventricular rate 120; orthopnœa, moderate œdema, gross clinical and radiological cardiac enlargement. No progress for 5 weeks on ordinary diet, full digitalisation, and occasional injections of mersalyl (total 8 ml.).

After 8 days on "salt-free diet" and a fluid intake averaging 3 litres (5½ pints) daily, she lost 2 kg. (4½ lb.). She lost another kg. in the next two weeks, but pitting œdema had not quite disappeared. Three injections of mersalyl 2 ml. on alternate days were followed by a rapid loss of a further 2 kg. (4½ lb.).

At this early stage of our investigation we regarded these results as encouraging. It was a novel experience to find that such quantities of fluid could be given with safety, and the initial improvement in the clinical condition was considered an achievement. We did not realise at the time the effect sodium restriction might have had in reducing the œdema, nor did we properly appreciate the benefit of mersalyl in these circumstances. Further cases have been treated successfully with "salt-free diet" and moderately high fluid intake (2–3·5 litres), but we soon found that suddenly "pushing" fluids in the acute stage of congestive heart-failure might be dangerous, even though sodium intake was rigidly restricted.

Case 3.—Male, aged 52. Cor pulmonale with moderate œdema. On ordinary diet with digitalis for 11 days, with average fluid intake 1·4 litres (2½ pints) daily, his œdema increased.

He was then put on "salt-free diet," and digitalis was stopped. After 2 days, fluids were increased to 3·5 litres (6 pints) daily. His condition became rapidly worse: he was restless, confused, disorientated, and grossly œdematous. There was no improvement during the next 48 hours. Mersalyl 2 ml. was then given, and he had a diuresis of 5·7 litres (10 pints) with a dramatic clinical improvement. Thereafter he lost 20 kg. (44 lb.), and his œdema cleared in 9 days on rest, "salt-free diet," and no drugs. His average daily fluid intake for this last period was 2·3 litres.

A second patient with cor pulmonale, who had responded slowly to "salt-free diet" and mersalyl on an average fluid intake of 2 litres (3½ pints) daily, was given a gastric drip of plain water whereby his daily fluid intake was raised to 6·5 litres (11½ pints) for two days. He too became extremely distressed, restless, and disorientated. On reversion of fluid intake to 2 litres (3½ pints), however, with two injections of mersalyl 2 ml. there was a pronounced clinical improvement, with loss of 5 kg. (11 lb.) in 5 days. Though the outcome in both of these cases was very gratifying, the clinical condition during the period of "forced" fluids was most alarming. A similar experience with 2 other patients, who were given mersalyl while taking extra

Digitized by Google

fluid, made us abandon "forced" fluid régimes in the acute state.

Meanwhile daily estimations of chloride loss had provided facts which changed our outlook on the whole problem. By raising the fluid intake on a low-sodium régime to 2·5–3 litres (5 pints) we could achieve an academic success, since the urinary output ran roughly parallel to the daily fluid intake, leading to a diuresis of 2·5–3 litres. But this watery diuresis was not always accompanied by an increase in chloride output or a decline in weight. Typically, the chloride concentration fell as the urinary output rose. When the changes in weight were plotted on a graph, the curve bore no constant relation to the fluid exchanges, provided the sodium intake was low. A very common finding was a gain in weight during the first few days, then a stationary period of variable duration—from 3 days to 3 weeks—followed by a gradual decline. In such circumstances mercury produced most spectacular results. Its effect could be observed on the weight curve, which showed a steep decline, and on the chloride excretion, which rose abruptly. The following case illustrates the sequence of events:

Case 4.—Female, aged 65. Hypertensive failure, blood-pressure 200/110, orthopnœa, gross œdema. Auricular fibrillation developed during observation. The patient was treated for 3 months with ordinary diet and digitalis plus occasional mercurials, with only slight improvement in œdema. During a preliminary observation period of 8 days on ordinary diet without digitalis, her weight rose from 46 kg. (7 st. 4 lb.) to 50·5 kg. (8 st.). Urinary chloride concentrations of up to 5 and 6 g. per litre were observed during this period. She was then kept on "salt-free diet" for 10 days, and her weight did not decrease. Urinary chloride concentration dwindled to less than 1 g. per litre on 6 of these 10 days, but water excretion was good throughout, running parallel to the intake and averaging 2·5 litres daily. After an injection of mersalyl 2 ml. the patient excreted 36 g. of chloride in 24 hours, and her weight fell by 3 kg. (6½ lb.) in 2 days (fig. 3; since the Fantus test does not measure concentrations of less than 1 g. per litre, the effect of mersalyl is somewhat exaggerated, but this does not affect the general trend observed in such cases).

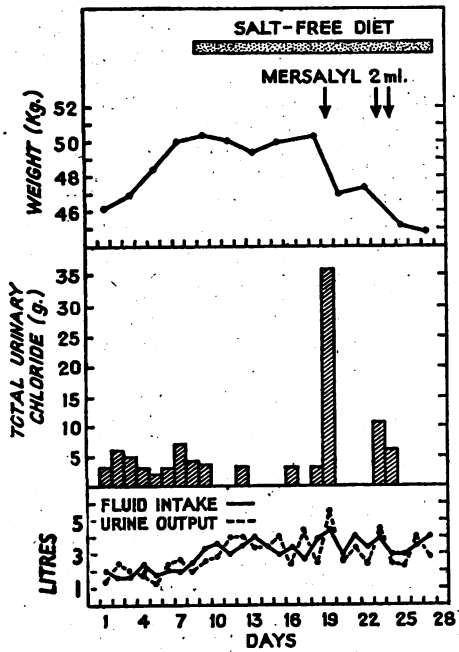


Fig. 3—Hypertensive failure (case 4), showing, on ordinary diet, rising weight with high but inadequate chloride excretion; and on "salt-free diet" plateau weight-curve with fall in chloride excretion despite urine output averaging 2·5 litres daily. Note injection of mersalyl followed by sharp increase in chloride output (36 g.) and steep fall in weight.

This is one of 10 similar observations, any one of which might have been chosen to illustrate the purely academic success of water diuresis in such circumstances. Perhaps, if we had persisted with the régime, our efforts would have been finally successful in some of the cases, but success is so much easier to achieve with mercury that we saw no point in withholding it.

Mercurial Diuretics

The most striking effect of a mercurial is seen in those cases in which a copious watery diuresis is paralleled by decrease in œdema and fall in weight. In some cases, however, there was little or no apparent water diuresis in response to mersalyl, but the increase in chloride output was nevertheless accompanied by a fall in weight.

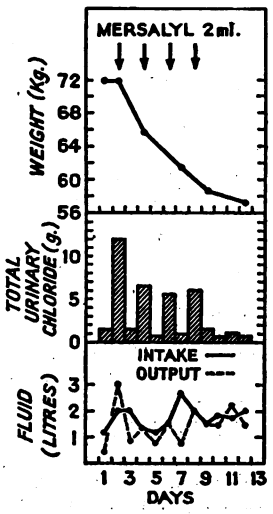


Fig. 4—Coronary disease with auricular fibrillation (case 5) on "salt-free diet" showing chloride diuresis in response to mersalyl with loss of œdema despite little apparent water diuresis.

Case 5.—Male, aged 79. Coronary disease: moderate œdema, auricular fibrillation, ventricular rate 120, blood-pressure 130/95. On "salt-free diet" and four injections of mersalyl 2 ml. he lost 14 kg. (30 lb.) in 10 days. There was no apparent water diuresis during this period except a moderate response after the first injection. His ventricular rate fell from 120 to between 70 and 80 without digitalis which was only prescribed just before his discharge (see fig. 4).

In some cases a single injection of mersalyl has a spectacular effect, clearing 6–9 kg. (13–20 lb.) of œdema fluid with a correspondingly high chloride loss. In others, however, the results are far from spectacular, each injection clearing only a small quantity of chloride with a correspondingly small drop in weight. Nevertheless, if the sodium intake is rigidly controlled, each gramme of chloride excreted represents a definite loss of œdema fluid which is not followed by a further accumulation, and with patience and persistence it is usually possible to achieve success in the most difficult cases. In these cases, when mersalyl was given on alternate days, we often noted that chloride was only excreted on the days of injection.

Another clinical observation emphasises the value of mersalyl. Many patients with congestive heart-failure complain, on admission, of thirst, and have a dry tongue; this is regarded as an indication of cellular dehydration, the patient in the words of Schemm being "brine-logged" rather than water-logged. Restriction of water intake has caused the extracellular fluid to become hypertonic (because the kidneys are provided with insufficient water to excrete the excess of salt) and water tends to be sucked out of the cells (Marriott 1947). Schemm (1944) further suggests that diuretics, by promoting water excretion, aggravate the condition. Our own experience hitherto showed that mercurials had a selective action on chloride excretion. It therefore seemed unlikely that cellular dehydration would follow from their use. We noted that dry tongue was relieved in our cases by a high-fluid and low-sodium régime and by mercurials with low sodium intake and fluid as desired. Pushing the investigation a step further we showed in three observations that dry tongue disappeared with a combination of mercurials and low-sodium and restricted fluid intake.

Like other workers, we have seldom observed toxic effects. During six months, 1325 ml. of mercurial diuretic was given to 114 patients in our wards. Two patients developed a rash:

In one a generalised morbilliform eruption appeared after the seventh injection of mersalyl 2 ml. Dimercaprol

Digitized by Google

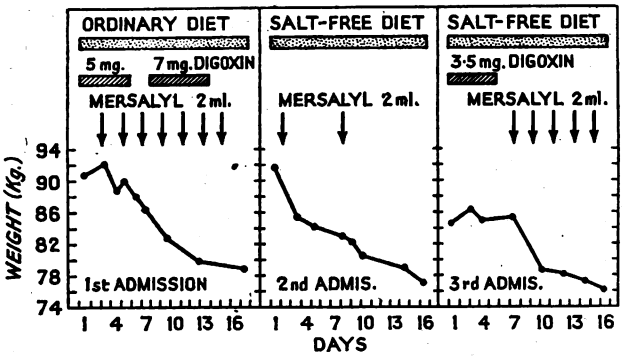


Fig. 5—Coronary disease, bundle-branch block, auricular fibrillation (case 6): first admission, patient becomes œdema-free on ordinary diet, digitalis, and 14 ml. of mersalyl; second admission, similar result obtained with "salt-free diet" and only 4 ml. of mersalyl; third admission, "salt-free diet" and digitalis produce no improvement, but subsequently there is a prompt response to mersalyl.

produced no obvious immediate benefit. Subsequently the patient improved and the rash was fading, but he collapsed and died 41 days after the rash had appeared. Kidney sections post mortem showed no evidence of acute degenerative change in the renal tubules.

A second patient developed itching erythema after the third mersalyl injection. This cleared in 4 days when mersalyl was discontinued, but recurred after a subsequent trial injection. Again it cleared in 4 days, and a slow uneventful recovery was made on "salt-free diet" alone.

We became so preoccupied with the action of mersalyl and its peculiar effect on sodium-chloride excretion that, on reviewing our observations, we noted that we had come to pay little attention to the value of digitalis in these cases. At the beginning we conformed to current therapeutic procedure but, without any planned or conscious effort to do so, we found we were relying on digitalis less and less, and in many cases omitting to prescribe it until œdema had cleared.

The main lines of treatment in the 64 cases discharged free of œdema were as follows:

Treatment	*"Salt-free diet"*	*Ordinary diet*
Rest alone	10	2
Rest and digitalis	5	3
Rest and mersalyl	25	6
Rest, mersalyl, and digitalis	11	2
Total	51	13

It will be noted that only a third of the cases received digitalis.

We have believed and we still believe that the functions of mercury and digitalis in congestive heart-failure are complementary. We did not arrange any part of the investigation for the purpose of comparing their effects. Nevertheless, data accumulated which left us with the impression that almost all our successes in the higher age-groups could have been gained without the use of digitalis, whereas most of them could not have been gained without mercury.

Case 6.—A man, aged 72, with bundle-branch block and auricular fibrillation, was first admitted on March 1, 1948, with gross œdema, ventricular rate 130. He was treated by rest, ordinary diet, digitalisation, and 14 ml. of mersalyl. He lost 12·8 kg. (28 lb.), became œdema-free in 14 days, and was discharged on March 30 on maintenance digoxin.

He was readmitted on May 4 in a similar condition as on March 1 (ventricular rate 100). On "salt-free diet" and mersalyl 4 ml., but no digitalis, he lost 14·8 kg. (33 lb.) and became œdema-free again in 14 days. On limited activity and "salt-free diet" he remained free from œdema in the ensuing week and was only digitalised just before discharge.

On his third admission on July 8, rest, "salt-free diet," and digoxin produced no improvement in 5 days. Digitalis was then stopped, and after five injections of mersalyl 2 ml. he lost 9·4 kg. (21 lb.) and became œdema-free in 10 days (fig. 5).

It should be noted that we are considering here only the short-term treatment of congestive heart-failure in hospital. As a routine we digitalised patients before discharge.

Mechanical Removal of Œdema Fluid

Mechanical removal of œdema fluid has declined in popularity since the introduction of mercurials. The treatment has obvious possibilities in certain cases. Theoretically, if sodium intake is rigidly controlled, no more fluid will accumulate in place of the fluid removed by tapping. Theoretical expectations have been well borne out in three observations. In one, a case of hypertensive failure in which progress was slow in spite of mercurials, abdominal paracentesis caused a sharp drop in weight and an improvement in the general condition. The weight did not rise again. The other two observations were made on patients in the acute dyspnœic stage, in both of whom mechanical removal of fluid by tapping probably saved their lives. The sustained loss of weight in all three cases showed that there was no further accumulation of fluid in place of the fluid removed.

DISCUSSION

As our investigation proceeded, there was inevitably a shift in emphasis from venous obstruction to sodium retention in our conception of the mechanism of congestive heart-failure. We confirmed the finding of Proger et al. (1942) that unlimited salt intake can bring about a relapse in convalescent cases. All therapeutic measures can be assessed by their effect on sodium retention. Thus, however gratifying it is to note the "emptying" of the neck veins and slowing of the heart after digitalisation, œdema will not disappear unless a negative sodium balance is induced at the same time. Again, large quantities of water can cure dry tongue in "brine-logged" patients and provoke a copious diuresis, but all this we found of little avail if chloride excretion was not maintained. In trying to reach a conception of the mechanism of sodium retention in these cases certain facts deserve special consideration. First, we found that all patients on admission, even the worst, were excreting 2–11 g. of chloride per litre of urine. Thus with a liberal intake of salt—e.g., 5–15 g. daily in an ordinary diet—the kidneys in congestive heart-failure will excrete sodium in moderately high concentration. If only chloride excretion remained at this level when salt is withheld from the diet, the treatment of such cases would be a simple matter. Unfortunately, as already noted, the tendency is for chloride excretion to fall, and in some cases chloride disappears from the urine on a "salt-free diet"—this, too, while the patient is œdematous.

In our conception of œdema, then, the mechanism which normally controls sodium metabolism is not completely thrown out of action but behaves as if it were geared to a level which accommodates a larger volume of extracellular fluid than the body normally tolerates. How this change in mechanism is mediated is not known. Merrill (1946), Merrill and Cargill (1947), Mokotoff and Ross (1947), and Mokotoff et al. (1948) have shown that in congestive heart-failure the glomerular filtration-rate may be reduced by as much as two-thirds by reduction of renal blood-flow. Tubular reabsorption of sodium is not increased. Hormonal changes, especially of the hypophyseal-adrenal cortical mechanisms, have been mentioned by Crutchfield and Wood (1948) and Dock (1948) as a factor of possible importance.

In the treatment of congestive heart-failure we have four important agents at our disposal, but it is no easy

Digitized by Google

matter to define the scope of each one of these. First, there is *rest*. In all cases rest is essential at the beginning of treatment. In old people, however, there is a tendency to become bedfast, which needs to be discouraged. Phlebitis and basal congestion are undesirable complications of prolonged absence of movement. Unless there are some important contra-indications, we like to start getting our patients up as soon as œdema has disappeared; no ill effects have been observed with this practice.

As regards the *diet*, it is difficult to decide how far salt should be restricted in a particular case. Sodium retention, whatever its mechanism and position in the cycle of events may be, has been established as a most important factor in congestive heart-failure. To rid the body of excess of sodium, output must exceed intake. In some cases increasing the output alone will achieve this object, but in most cases to expedite the process some restriction of intake will also be necessary. In general the more severe the case, the more rigid this restriction will need to be.

Some restriction of intake has been advocated by most physicians for many years. Wheeler et al. (1947) have classified diets according to salt content as follows:

(1) Average diet, without salt restriction, 6–15 g.
(2) Average diet, without salt added at table, 4–7 g.
(3) Average diet, without salt added in cooking, 3–4 g.
(4) Low-sodium diet, 1–2 g.

The crucial difference between the types 3 and 4 lies in salt-free bread: 9 oz. of ordinary bread contains 2·5–3 g. of salt.

Most textbooks now recommend a diet of type 3, The chief criticism of such a diet is that it is dull, and its use "savours of treating the disease rather than the patient" (*Lancet* 1946). Such diets are indeed dull, and unfortunately, so far as we have observed, there is no efficient substitute for salt. We maintain, however, that type 3 is just as dull as type 4. Therefore, so far as short-term treatment in hospital is concerned, we have no hesitation in advocating type 4 in all cases until œdema has cleared.

In maintenance therapy there are domestic difficulties in addition to the dullness: salt-free bread may be hard to get, and a "salt-free diet" may entail extra cooking which will not be welcomed by the overburdened housewife. In a case of average severity the patient must therefore choose between the difficulties and dullness of salt restriction and the discomfort of more frequent injections of mersalyl. In practice we explain the problem to each patient before his discharge, and the decision rests with him.

To the question of how much fluid should be consumed the patient again may generally be left to provide the answer.

We have been puzzled by the alarming results of "forcing" fluids above 3·5 litres in the acute stages of congestive heart-failure. According to Schemm (1944) 80% of his patients were given 4–7 litres daily without ill effects. This high intake was largely achieved with isotonic intravenous supplements. Three of our patients received gastric drips; but, though they all became extremely ill and distressed, there was no vomiting or evidence of abdominal distension. We are satisfied that in our cases the sodium intake was adequately restricted, and we wonder whether the administration of mercurial diuretics explains many of the good results claimed by Schemm for his high-fluid therapy. However, two of our patients received mersalyl in addition to the forced fluid intake, and this did not obviate the distressing symptoms noted.

Mercurial diuretics are a powerful aid in the treatment of congestive heart-failure, because of their selective action on sodium-chloride excretion. Roby and Pfeiffer (1941) found that in dehydrated dogs the administration of a mercurial was often followed by a chloride diuresis without a water diuresis. They used the chloride rather than the water excretion as a test of therapeutic (or pharmacological) efficiency. Crutchfield and Wood (1948) found that mercurophylline injections disproportionally increased urinary volume and total renal sodium excretion, favouring the latter. They suggest that the primary renal action of these mercurials may be depression of tubular reabsorption of sodium.

Since diuresis is popularly held to refer to water excretion only, to say that mercury is an efficient diuretic describes only half or less than half its pharmacological action. Not only did we find that copious water diuresis per se might be useless, but also we noted that a high salt excretion with loss of weight was not necessarily accompanied by apparent water diuresis.

Lastly, there is *digitalis*. Our limited experience does not permit us to run counter to accepted procedure, in which the exhibition of digitalis is indicated in all cases of congestive heart-failure of the "low output" type (McMichael 1947). We have observed many cases of recovery in congestive heart-failure with rest and digitalis alone, but in this investigation we have seen cases in which digitalis did not eliminate sodium and reduce œdema in cases which responded successfully to mersalyl in both respects. These cases were not congestive heart-failure of the "high-output" type (cor pulmonale, anæmia, Paget's disease) in which, as McMichael (1947) and his colleagues have suggested, digitalis is unlikely to be successful. So far as we could judge, digitalis has no specific effect on sodium metabolism, and the good results following its use in many cases probably derive from its beneficial effect in reducing venous pressure. This may be insufficient to effect recovery in advanced stages of congestive heart-failure.

In the ordinary course of events the question of whether mercury is superior to digitalis does not arise. If fluid has been removed mechanically, if sodium restriction is rigidly maintained, if digitalisation is complete and successful, less mercury will be required.

After the œdema has cleared, each case presents a nice exercise in clinical judgment. At one extreme is the intelligent coöperative patient who will do well on salt restriction only; at the other is the mildly demented old person who will need digitalis and regular injections of mersalyl.

SUMMARY

Clinical observations, with particular regard to fluid and salt exchanges, have been made during six months on 107 patients with congestive heart-failure.

In the acute stage a low-sodium diet, with fluid intake as the patient desires, is advocated. "Forcing" fluid intake above 3·5 litres has in our experience proved dangerous in this stage.

Salt excretion can be accelerated, with or without a water diuresis, by giving mercurials. The special value of the latter in treatment derives from this pharmacological action.

Cellular dehydration in "brine-logged" œdematous patients has been clinically relieved by low-sodium diet and mersalyl, even with restricted fluid intake.

Practical measures of salt restriction for patients in hospital and at home are discussed.

We have pleasure in acknowledging the help received from many members of the staff of Belmont Road Hospital, and also from Dr. J. I. Gibson, of the pathological department, Liverpool University.

REFERENCES

Burch, G. (1947) see *J. Amer. med. Ass.* **133**, 19.
Crutchfield, A. J. jun., Wood, J. E. jun. (1948) *Ann. intern. Med.* **28**, 28.
Dock, W. (1948) *Ibid*, **33**, 11.

Continued at foot of next page

Digitized by Google

SUBCUTANEOUS IMPLANTATION OF INSULIN IN DIABETES MELLITUS*

LUIS VARGAS
M.D. Santiago
PROFESSOR OF PATHOLOGICAL PHYSIOLOGY, CATHOLIC UNIVERSITY OF CHILE

USING the method, introduced by Deanesly and Parkes (1937), of subcutaneous implantation of fat-soluble hormones, Vargas et al. (1944) proved in the normal rabbit that implanted pellets of protamine-zinc-insulin complex (P.Z.I.) mixed with cholesterol gave up their insulin slowly. This observation showed that the chemical combination of protamine with insulin was more important than the physical mixture with cholesterol, the absorption of P.Z.I. alone being very slow. The importance of this conclusion is enhanced by the fact that in previous experiments normal rats implanted with pellets of insulin-cholesterol died (Parkes 1942). In the rabbit made diabetic with alloxan (Dunn et al. 1943, Bailey and Bailey 1943) or with alloxantin (Koref et al. 1944) we showed the great effect of implants of pellets of P.Z.I.-cholesterol (Vargas et al. 1948). Of 23 rabbits 12 were used as controls to show the spontaneous course of alloxan diabetes and 11 were treated with different insulin implants. P.Z.I. mixed with an equal amount of cholesterol proved the most effective, in doses which gave 430–690 units of insulin per kg. of body-weight, in controlling the diabetes without the aid of ordinary injections of insulin. The animal which reacted best was that which, after nine months' severe diabetes, recovered completely with a second implant of insulin. None of the controls showed such recovery.

I report here the results obtained in the first seven patients treated by this new method of administering insulin.

METHOD

Preparation of Pellets.—The material for making the pellets was obtained from the complex of P.Z.I. precipitated by addition of the buffer solution. This emulsion was filtered, and the residue from the filter paper was dried in vacuo, powdered, and mixed with an equal amount of cholesterol (Phanstiehl Chemical Co.) after both substances had been passed through ether. This powdered P.Z.I. contained 8·6–17 units of insulin per mg. Uniform compression was obtained by using a special machine. During all the stages the greatest care was taken over asepsis; the instruments and working surfaces were always sterilised over a flame. The pellets thus prepared weighed 3–14 mg. and measured 1·5 mm. across and 2–10 mm. long. In cases 6 and 7 pellets 3 mm. in diameter were used.

Calculation of Implant Dose.—On the basis of the experimental observations in rabbits we calculated the daily absorption to be about 1% of the amount implanted. The implantation was done with a trocar and procaine locally, in the subcutaneous cellular tissues of the thigh, gluteal, or dorsal regions.

Preparation and Study of Patient.—Control of the blood-sugar level was attempted with diet and P.Z.I. injections to determine the daily requirement of insulin. The daily carbohydrate intake was 90 g. (one case), 160–180 g. (five cases), and 230 g. (one case). In four cases the injections of insulin were stopped completely after implantation of the pellet. In the other three they were diminished in accordance with previous calculations and with the patient's reaction to the implant. Blood-urea, glycosuria, diuresis, and body-weight curves were used to study the evolution of the diabetes. The blood-urea was determined by the ferricyanuric method, and the glycosuria by Fehling's method.

ILLUSTRATIVE CASE-RECORDS

Seven patients have been treated with the subcutaneous implants of P.Z.I.-cholesterol. We have summarised the most illustrative cases, and the chief data are given in the accompanying table.

Case 2.—An obese woman, aged 44, with diabetes accentuated by menopause and complicated by severe suppurating gangrene of the left foot, had lipodystrophy of the extremities, mild diabetic retinopathy, and anæmia. Her insulin requirement was studied for 22 days. Owing to her obesity a regimen of 90 g. of carbohydrate was started. The hyperglycæmia and glycosuria were abolished with 50 units of P.Z.I. Three days before the implant the injections of insulin were stopped, whereupon the blood-sugar level rose and glycosuria reappeared.

On Sept. 1, 1947, insulin 2123 units (P.Z.I.-cholesterol 265 mg.), was implanted in the right gluteal region. With this dose it was hoped to release about 25 units daily. The site of the implant showed a foreign-body reaction, which regressed slowly. Fig. 1 shows the influence of the insulin implant, which in this instance is clear enough because the injections of insulin had been stopped. Two subsequent implants of insulin 1484 units (P.Z.I.-cholesterol 180 mg.) and insulin 2975 units (P.Z.I.-cholesterol 350 mg.) were given to bring the blood-sugar level down to normal. The third implant did not produce a local reaction. Glycosuria disappeared on the fifth day after the original implantation. The clinical course was excellent, the gangrenous wounds healed, the pedal pulse returned, and the skin temperature was restored to normal.

The patient was discharged 159 days after the first implantation of insulin, using her foot without difficulty. She was taught how to use Fehling's test for glycosuria, and 37 days later, when readmitted to hospital, she said she had had glycosuria only one day. The blood-sugar level during her second stay in hospital was 130–150 mg. per 100 ml. and there was no glycosuria. She left the hospital in very good condition 227 days after the original implantation; her blood-sugar level was then 140 mg. per 100 ml., and she had no glycosuria. At 235 days she remained in the same condition. The exudative patches on the retina had disappeared.

Case 5.—A man, aged 42, who in the last two years had lost 30 kg. in weight, had polyuria, polydipsia, and polyphagia, and a history of syphilis, with positive Wassermann and Kahn reactions, aortitis, and signs of tabes dorsalis. On admission he was in poor health, pale, asthenic, and with intense pain in the legs. Treatment was begun after he had been without insulin for 16 days. A diet of 180 g. of carbohydrate and 30 units daily of the mixture of 1 part P.Z.I. and 2 of insulin, later 40 units, produced a favourable change in weight, hyperglycæmia, and glycosuria. Liver extracts were added. On Feb. 6, 1948, in ulin 3400 units (P.Z.I.-cholesterol 400 mg.) was implanted in the right thigh. This implant was calculated to deliver 100% of the previous daily dose of insulin. P.Z.I. 10 units was injected during the first four days, after

* This work has been done with the collaboration of the Clinical Hospital of the Catholic University. A preliminary communication was made to the Medical Society of Santiago, with the first three cases, in December, 1947. We include those cases since the follow-up is now more complete.

DR. REID, DR. HUGHES: REFERENCES—*continued*

Fantus, B. (1936) *J. Amer. med. Ass.* **107**, 14.
Karell, P. (1866) *Arch. gén. Med.* **2**, 513.
Lancet (1946) ii, 54.
Landis, E. M., Brown, E., Fauteux, M., Wise, C. (1946) *J. clin. Invest.* **25**, 237.
Leiter, L. (1948) *Ann. intern. Med.* **28**, 229.
McCance, R. A., Widdowson, E. M. (1946) The Chemical Composition of Foods. London.
McMichael, J. (1947) Advances in Internal Medicine. New York; vol. II, p. 64.
Marriott, H. L. (1947) *Brit. med. J.* **1**, 285.
Merrill, A. J. (1946) *J. clin. Invest.* **25**, 389.
— Cargill, W. H. (1947) *Ibid*, **26**, 1190.
Mokotoff, R., Ross, G. (1947) *Ibid*, p. 1190.
— — Leiter, L. (1948) *Ibid*, **27**, 1.
Proger, S., Ginsburg, E., Magendantz, H. (1942) *Amer. Heart J.* **23**, 555.
Roby, C. C., Pfeiffer, C. (1941) *Amer. J. Physiol.* **135**, 591.
Schemm, F. R. (1942) *Ann. intern. Med.* **17**, 952.
— (1944) *Ibid*, **21**, 937.
Schroeder, H. A. (1941) *Amer. Heart J.* **22**, 141.
Warren, J. V., Stead, E. A. jun. (1944) *Arch. intern. Med.* **73**, 138.
Wheeler, E. O., Bridges, W. C., White, P. D. (1947) *J. Amer. med. Ass.* **133**, 16.

Digitized by Google

which it was stopped. The clinical course was excellent for 69 days (fig. 2), except that, 13 days after the implantation, the patient developed a severe choleriform diarrhœa, became dehydrated, and lost 8 kg. of weight. He was treated in the usual manner, without additional injections of insulin, and regained his weight in 13 days. He left the hospital in good health and 8 kg. heavier than when he arrived.

He did not return for his weekly examination but reappeared 146 days after the implantation, with a blood-sugar level of 256 mg. per 100 ml., a glycosuria of 20 g. per litre, and a loss of 6 kg. in weight. He said the characteristic symptoms of diabetes had reappeared 15 days previously, and the diarrhœa had relapsed from time to time. He was readmitted and received a second implant of insulin, 4350 units (P.Z.I.-cholesterol 530 mg.), which produced equally good results.

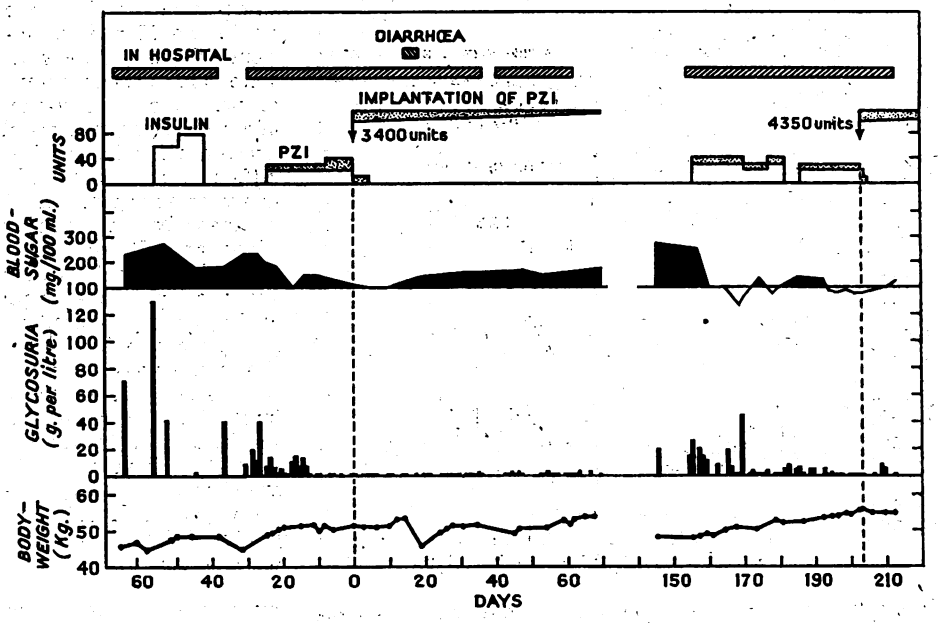


Fig. 2—Fairly mild diabetes easily controlled by insulin (case 5). The two implants were calculated to supply 100% of the daily requirement: the first on a basis of 1% daily absorption, and the second 0·7%. Outside the hospital the glycæmia tends to rise, probably owing to the uncontrolled diet. The patient was readmitted to hospital in the same diabetic condition as on his first admission, and was controlled with the same dose of insulin.

Case 7.—A child, aged 10 years, with very severe diabetes, which had suddenly appeared in July, 1946, had had four diabetic comas, each on the second day after injections of insulin had been stopped. His daily requirement of insulin had been 80–140 units throughout 1946–47 and 180 units during 1948. We confirmed that the daily requirement of insulin was 180 units (two daily injections) and the strong tendency to glycosuria. On May 21, 1948, the patient was given a subcutaneous implant of insulin 16,850 units (P.Z.I.-cholesterol 2030 mg.) in the left dorsal region. He was up and about all the time, often leaving the hospital during the day.

Since this was the biggest implant we have given, the urine was tested every four hours during the day. The insulin injections were stopped on the 5th day after implantation. Fig. 3 shows the results. A striking general reaction was followed by a gain of 1·5 kg. in weight. The local tolerance was good, in view of the large amount implanted. A swelling, accompanied by extrusion of two pellets and some yellowish liquid, was seen 7–9 days after the implantation. A felon appeared on the left little finger 20 days after implantation, and 30, 50, and 80 units of P.Z.I.-insulin were injected during the next few days. The boy continued growing and was $1^1/_2$ in. taller than on admission; his appetite was excellent.

On the 48th day after the original implantation insulin 10,000 units (P.Z.I.-cholesterol 1250 mg.) was implanted in the right dorsal region. The standard hospital diet, containing about 180 g. of carbohydrate, was substituted for the diabetic diet. It was hoped to be able to give by implantation 100% of the new daily requirement of insulin, and it looked as if we could, because the child remained without insulin from the 5th day after the second implantation and the blood-sugar level was 125, 118, 118, and 119 mg. per 100 ml. during the last 20 days of observation. However, 6 days later the diabetic symptoms reappeared and the boy was readmitted; but it should be remembered that he was not then on a diabetic diet.

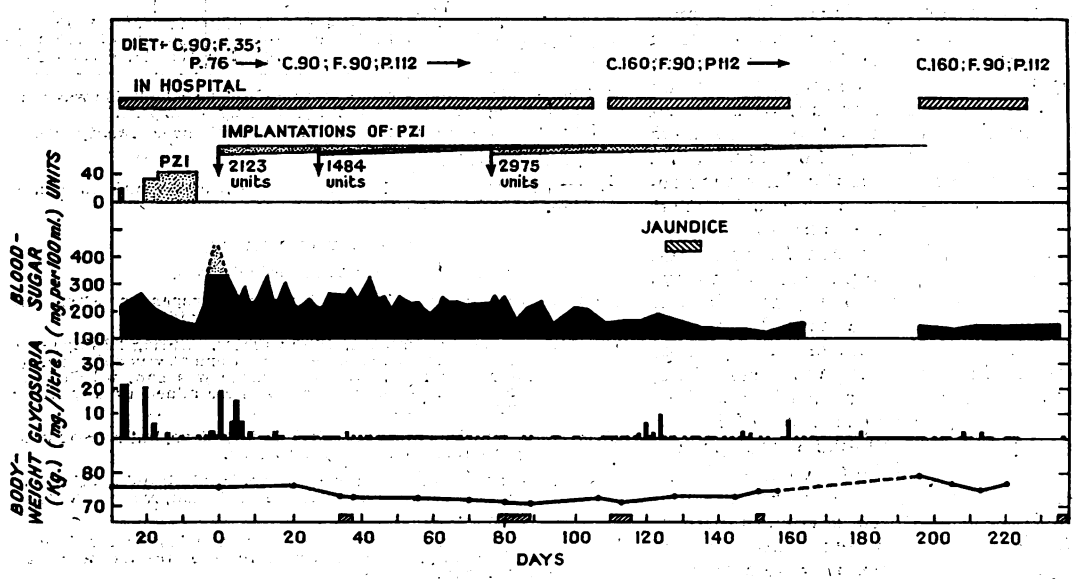


Fig. 1—Diabetes complicated by a suppurating gangrene of the foot (case 2). Note that after the implant no more insulin was injected, in spite of the fact that the implant was calculated to supply only 25% of the daily requirement. Aglycosuria was reached on the 6th day, though the glycæmia remained about 250 mg. per 100 ml. 105 days after the first implant the patient was discharged with her foot cured. It is calculated that 100% of the daily requirement was supplied after the third implant. Glycosuria: a line marked at O signifies that it was negative; if there is no line, the glycosuria was not determined. The same applies to the other charts. C, carbohydrates; F, fats; P, proteins. A rectangle on the lower abscissa indicates a menstrual period.

RESULTS

The daily requirements of insulin before the implantation of P.Z.I.-cholesterol were 40–180 units. The accompanying table shows the percentages of the daily requirement supplied by the implants. It

Digitized by Google

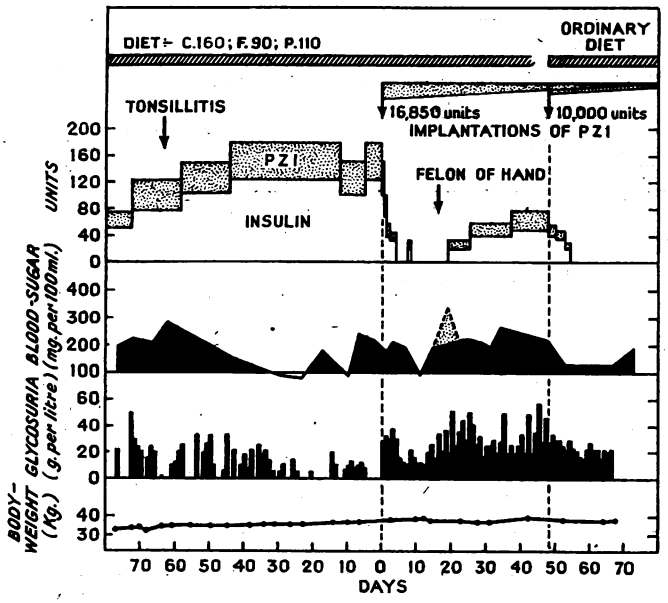


Fig. 3—Juvenile diabetes resistant to insulin (case 7). Before the implantation there was a high insulin requirement (180 units in two daily injections), with a small margin of useful dose (150 units proved insufficient) and a persistent glycosuria. The two implantations demonstrated the slow absorption of insulin, because in spite of the high doses implanted (16,850 and 10,000 units respectively) there was no hypoglycæmia, and decreasing doses of insulin were injected the first 4 days. Though the first implant did not prove sufficient for more than 20 days its effect persisted, because even though the second implant was smaller than the first it supplied 100% of the daily requirement for 26 days. Further, before the second implantation only one daily injection of insulin was administered and the dose was considerably lower (60-80 units).

can be concluded that the results were in accordance with the calculation based on the daily rate of absorption of insulin implanted. The only exception was case 3 after the second implantation, and this was the only case where an abscess formed at the site of implantation, with the extrusion of two pellets.

We believe that cases 2, 5, and 7 are especially informative. It is highly significant that in case 2 the gangrene of the foot healed without additional treatment, in spite of the first implant only supplying 40% of the daily requirement of insulin and the injections being stopped on the day of implantation. In cases 5 and 7 insulin injections were also stopped—in case 5 during the whole follow-up after implantation. It is significant that, on readmission, 155 days after implantation, case 5 said his diabetic symptoms had reappeared only 25 days previously. In case 7, even though the 16,850 units implanted did not supply so much of the daily requirement of insulin as we had hoped, it is noteworthy that from the 5th to the 20th day after implantation no insulin was injected. The blood-sugar level fell to 90 mg. per 100 ml.; whereas previously the patient had always fallen into a diabetic coma on the 2nd day after insulin injections were stopped. With the second implant, given 28 days later, the boy had a normal blood-sugar level, little glycosuria, and an excellent general condition, even though he was not maintained on a diabetic diet. Case 7 shows definitely the slow absorption of insulin from subcutaneous implants of P.Z.I.-cholesterol pellets.

The local tolerance of the implants varies. Of 11 implants 1 formed an abscess which drained pus and pellets, healing rapidly; 2 produced a small puriform collection; and 8 were well tolerated, like the fat-soluble hormones. In 2 cases a few pellets were extruded.

DISCUSSION

Cutting et al. (1941) tried a mixture of insulin and cholesterol in equal parts in pellets of 100–200 units. The results varied in six pancreatectomised dogs observed up to the 13th day. Several animals died of hypoglycæmic shock. These workers concluded that clinical trials were too risky. Our observations agree that the absorption of pellets of insulin-cholesterol is rapid, characteristic of a mixture of a water-soluble substance with cholesterol. On the other hand, the absorption of P.Z.I. is entirely different, because P.Z.I. is a compound which is insoluble in water at the pH of the tissues, and implanted subcutaneously is absorbed very slowly (Vargas et al. 1944). Mark and Biskind (1940) concluded that the effect of implanted pellets of P.Z.I. lasted only 44–100 hours. But their pellets were prepared by a simple mechanical mixture of crystallised zinc-insulin with protamine and not by a previous combination in solution to obtain the complex—i.e., the insulin remained as a water-soluble substance. This explains why they could not implant higher doses without producing hypoglycæmic shock, and their wrong conclusion that pellets of true P.Z.I. (obtained from the commercial solution), which are absorbed slowly, were inactive. In fact these pellets were not inactive, since a solution of one such pellet produced hypoglycæmic action. However, the pellets were without insulin effect, because of the low doses

SUBCUTANEOUS IMPLANTATION OF PELLETS OF PROTAMINE-ZINC-INSULIN PLUS 50% OF CHOLESTEROL

Case no.	Sex	Age (years)	Days of observation		Daily insulin injected (units)		Amount of daily requirement supplied by implant*			Amount implanted		
			Pre-impl.	Post-impl.	Pre-impl.	Post-impl.	Calc.		Obtd	Total		Per kg.
							Units	%	%	mg.	u.	u.
1	F	45	60	89	60	40	15	25	25	350	1535	35·7
2	F	44	28	235	50	0	20	40		265	2123	28·3
							15	30		180	1484	20·0
							30	60		350	2975	41·9
								100	100			
3	F	21	10†	130	80‡	40	30	38	50	350	2870	60·0
						40	20	25	25	248	2040	40·8
								60	25			
4	M	42	85	35 (83)	120	70	50	42	42	586	5100	92·7
5	M	42	66	69 (146)	40	0	34	100	100	400	3400	65·4
6	F	50	57	54	?	45	19	..	..	327	1900	..
7	M	10	80†	67	180‡	0	168	93	90	2030	16850	450·0
							100	100	100?	1250	10000	250·0

* Calc. = calculated; obtd. = obtained. The calculation was made on the experimental basis of 1% of daily absorption.

† Case 3 has been under medical control over twenty years; case 7 for two years.

‡ Two daily injections.

Figures in parentheses in above columns correspond to control outside the hospital.

SUMMARY OF RESULTS

Case 1.—Good, corresponded to our calculations.

Case 2.—Very good; insulin injections suspended after first implant; aglycosuria was reached rapidly.

Case 3.—The second implant, 46 days later. During 32 days after implantation, 50% of daily requirement was obtained, but later only 25%. Local tolerance was bad, with abscess formation. Insulin injections were added usually in one daily injection.

Case 4.—Insufficient to suspend insulin injections, but corresponded approximately to our calculations.

Case 5.—Very good. Completely replaced insulin injections. Readmitted 155 days after implantation, received a second implant.

Case 6.—It was impossible to determine the insulin requirement before implantation, therefore the results were not conclusive.

Case 7.—Very good during the first twenty days, after which it was necessary to add insulin injections (only one daily). Second implant, 48 days later, supplied about 100% of the daily requirement without diabetic diet, until the 26th day, when the diabetic symptoms reappeared, necessitating readmission to hospital.

Digitized by Google

implanted, insufficient for reducing the blood-sugar level.

The doses implanted in man have been low in comparison with those used in the rabbit. Nevertheless case 7 is an important exception, since the enormous dose of 450 units per kg. of body-weight was required in the first implant, a similar dose to that used in the alloxan-diabetic rabbit.

The pellets were prepared aseptically so far as possible, though not in an atmosphere of sterilised air. The degree of compression, though fairly uniform in the smaller pellets, has varied greatly in the larger ones. Obviously all this can be improved.

The effect of insulin implants has been excellent. We cannot yet state the exact duration, but it has been about the calculated time of 80–100 days, according to the 1% daily absorption-rate. We emphasise that massive absorption has never taken place, and therefore there is no danger of hypoglycæmic shock, so long as we consider the relationship we have established between the requirement and the absorption. The complex of P.Z.I. alone is absorbed just as slowly as P.Z.I.-cholesterol: hence, even if some of the pellets were to break, there would be no risk; the only effect would be to increase the absorption area slightly.

This new way of administering insulin will not only abolish daily injections but also may achieve better results. The latter is understood if one remembers that the implant continuously gives out insulin, imitating the effect of an artificial endocrine pancreas, thus preventing an endocrine disorder and perhaps restoring the pituitary-pancreas relationship.

SUMMARY

The application to human diabetics of the results of the corresponding experiments on animals has been tested.

In the seven cases presented here it was shown that pellets of protamine-zinc-insulin-cholesterol, implanted subcutaneously, are absorbed as slowly as fat-soluble hormones.

The dose used in the implant varied from 20·0 to 92·7 units of insulin per kg. of body-weight, except in one case in which 450 units was given.

It was calculated, in accordance with experimental data, that the daily absorption of the implant was about 1%, which seems to be confirmed by the present cases. This assures a maximum duration of activity of the implant of about 100 days.

We consider that the method of implanting pellets of insulin used by us is extremely promising and worth further study with a larger number of patients.

All the cases, except case 1, were seen at the Clinical Hospital of the Catholic University. The Hospital del Salvador has collaborated in cases 1, 2, and 5; and the Hospital Arriarán and the Hospital San Borja in case 7. I am very grateful for the coöperation of the professional and technical personnel of these institutions, particularly to Prof. C. Lobo Onell. Thanks are also due to my assistants from the department of pathological physiology for their valuable collaboration and to the Institute M. T. Sanitas for the protamine-zinc-insulin.

REFERENCES

Bailey, C. C., Bailey, O. T. (1943) *J. Amer. med. Ass.* **122**, 1165.
Cutting, W. C., Morton, M. C., Cohn, R. B. (1941) *Endocrinology*, **28**, 679.
Deanesly, R., Parkes, A. S. (1937) *Proc. roy. Soc.* B, **124**, 279.
Dunn, J. S., Kirkpatrick, J., McLetchie, N. G. B., Telfer, S. V. (1943) *J. Path. Bact.* **55**, 245.
Koref, O., Vargas, L. jun., Rodriguez, F. H., Telchi, A. (1944) *Endocrinology*, **35**, 391.
Mark, J., Biskind, G. R. (1940) *Ibid*, **26**, 444.
Parkes, A. S. (1942) *J. Endocrinol.* **3**, 220.
Vargas, L., Koref, O., Lewin, J. (1948) *Bol. Soc. Biol. Santiago*, **5**, 32.
— — Zañartu, J. (1944) *Ibid*, **1**, 90.

COMPLETE RUPTURE OF THE MEMBRANOUS URETHRA

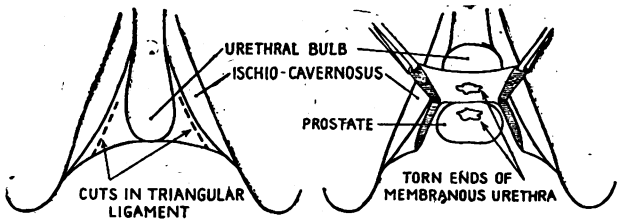
FOLLOW-UP NOTE

ALAN H. HUNT
D.M., M.Ch. Oxfd, F.R.C.S.
ASSISTANT SURGEON, ST. BARTHOLOMEW'S HOSPITAL AND THE ROYAL CANCER HOSPITAL, LONDON

C. NAUNTON MORGAN
M.B. Lond., F.R.C.S.
SURGEON, ST. BARTHOLOMEW'S HOSPITAL, ST. MARK'S HOSPITAL, AND HOSPITAL FOR TROPICAL DISEASES, LONDON

IN 1942 we reported [1] a case of complete rupture of the membranous urethra treated by anastomosis without an indwelling catheter. A post-office jointer, aged 24, sustained a comminuted fracture of the pelvis on Jan. 26, 1941, and was operated on four hours after admission to St. Bartholomew's Hospital, when he had recovered from the shock of the injury.

The bulb of the urethra was hinged forwards by dividing the triangular ligament posteriorly between the ischiocavernosus and bulbocavernosus muscles, thus enabling the two ends of the torn membranous urethra to be sutured by direct end-to-end anastomosis. The patient had been placed in the lithotomy Trendelenburg position, and the approximation of the two ends was facilitated by the assistant pressing the prostate down into the perineal wound. The bladder was drained suprapubically for 15 days. A catheter was passed on the 19th day, and removed on the 21st, by which time the suprapubic cystotomy had healed. The patient then passed urine normally. Gum-elastic bougies were passed 1, 2, 3, 6, and 15 months after the accident, but never was a stricture encountered. The pelvic fractures healed satisfactorily, and the patient returned to heavy work. Later he joined the Army and was passed fit for service overseas. On demobilisation he returned to his old job. The last time an instrument was passed was on April 9, 1942. He has had



Exposure of ruptured membranous urethra.

no difficulty or disturbance of micturition, and there has been no interference with sexual function. He is now married and has two children. He regards himself as a perfectly normal man.

We feel that the eminently satisfactory outcome in this case invited a brief note. Neither of us has since had the opportunity of treating a similar case. It will be realised that the operation must not be attempted on a severely shocked patient. We emphasise the following points: (1) the exposure of the membranous urethra in this operation is excellent; (2) the omission of an indwelling catheter, together with accurate end-to-end suturing, appears not only to have enabled the urethra to heal without producing a stricture, but also to have eliminated the peri-urethral and periprostatic fibrosis which occurs in these cases with concomitant incontinence or sterility; and (3) the incisions in the triangular ligament, carefully done, do not damage the nerves supplying the bulb of the urethra.

It has been proposed by Millin [2] that as good an exposure could be obtained by the retropubic approach.

1. Hunt, A. H., Morgan, C. N. *Lancet*, 1942, ii, 330.
2. Millin, T. Retropubic Urinary Surgery. Edinburgh, 1947; p. 174.

Digitized by Google

Our experience of total cystoprostatectomy for carcinoma of the bladder has shown us that this is not so, and that the membranous urethra can be exposed far better through the perineum than retropubically.

FILAMENTOUS FORMS ASSOCIATED WITH NEWLY ISOLATED INFLUENZA VIRUS

C. M. CHU * M.B. Shanghai, Ph.D. Camb.
I. M. DAWSON Ph.D. Glasg.
W. J. ELFORD Ph.D. Brist.
From the National Institute for Medical Research, London, N.W.3

With illustrations on plate

THE epidemic of influenza that has spread across Europe in recent months has provided the opportunity of studying freshly isolated virus from widely separated localities and making comparisons with the known classical A and B strains. This note reports observations on the morphological characters exhibited by recently isolated virus passaged amniotically and allantoically in fertile hens' eggs.

We have taken electron micrographs of specimens prepared by the new technique of adsorption on the membrane of fowl erythrocytes described by Dawson and Elford (1949a). Virus is adsorbed directly from freshly harvested allantoic or amniotic fluid, and the cell-ghosts may be sedimented in the centrifuge in a few minutes at 500 r.p.m., so that washings before and after fixation with osmic acid are quickly effected. The final aqueous suspension for electron microscopy is thus produced without subjecting the material to harsh manipulation. A representative picture of the adsorbable elements is obtained, and this may, under controlled conditions, be interpreted quantitatively.

With the active collaboration of our colleagues Drs. C. H. Andrewes, T. H. Flewett, and A. W. Gledhill we have been able to examine the infective fluids from the earliest egg passages of strains sent to the laboratory of the World Influenza Centre, in this institute, from cases of influenza in Italy, France, Holland, Czechoslovakia, and England. Electron micrographs of the classical A and B strains of influenza show the virus as round bodies $90 \pm 11 \cdot 5$ mμ and 103 ± 8 mμ in diameter respectively.

Mosley and Wyckoff (1946) reported that they had observed elongated forms associated with several A and B strains of influenza virus passaged in eggs. We have confirmed these observations for PR8 (A) and Lee (B) strains, using the red-cell membrane adsorption technique (fig. 1). The elongated forms were, however, very few compared with the round elementary bodies and were not consistently encountered. The temptation was to dismiss them as artefacts or material having nothing to do with the virus. This problem of the long forms, however, clearly had to be faced seriously when we observed long filamentous forms with a strain of fowl-plague virus adsorbed on the red-cell membrane (Dawson and Elford 1949b.)

The first of the recently isolated influenza viruses to be examined was allantoic fluid of the A/Nederland I/49 strain after three egg passages. The electron micrographs revealed long filamentous forms, rods of intermediate length, and round or slightly ovoid elementary bodies (figs. 2–4). The numbers of elongated forms adsorbed were often comparable with the numbers of elementary bodies, in striking contrast to their paucity in preparations of the old PR8 and Lee strains. Similar photographs, with some variation in the average lengths of the long forms and their numbers relative to the elementary bodies, were obtained from twelve virus isolations.

* Working at the World Influenza Centre (W.H.O.).

IDENTITY OF LONG FORMS

The question immediately arises: "Are these long forms influenza virus?" We are not yet certain of the answer. It is only possible here to summarise some relevant observations, which must be elaborated and discussed more fully later.

(1) That the long forms seen in electron micrographs are not artefacts produced by drying or derived from the laked fowl cells is proved by the fact that the filamentous forms may be seen in untreated allantoic fluid with a good dark-ground microscope—i.e., Zeiss 'Cardioid' ultramicroscope. Yet another means for their quantitative study is thus provided.

(2) No filamentous forms have been observed directly in, or seen in micrographs of, normal allantoic fluids of 10–13 day eggs. Heinmets and Golub (1948) have shown that fibrillar structures may be derived from the normal cells of allantoic membranes. These exhibited the banded structure with 64 mμ spacing characteristic of collagen. The long forms of our influenza preparations have not possessed this banded structure but have had all the appearances of genuine growth processes, with internal structures often evident. Only in one instance out of numerous preparations carefully examined has a banding with a 64 mμ spacing been observed.

(3) Virus has been passed through the tightest gradocol membranes likely to permit passage of influenza virus. The filtrates inoculated into eggs have yielded both long and round forms. This suggests that the elementary body can give rise to the elongated forms when grown in a suitable environment.

(4) The filaments and round elementary bodies are adsorbed on and eluted from the red-cell membrane. When heat-inactivated virus was adsorbed on the fowl red-cell membranes at 0°C it did not spontaneously elute; but, when it was incubated with ferret antisera at 37°C, the homologous antiserum removed both long and round forms from the membrane. With heterologous sera of the classical A (PR8) and B (Lee) strains a considerable portion remained adsorbed.

(5) We examined, in the cardioid ultramicroscope, mixtures of A/Paris PLI/49 virus with (*a*) homologous ferret antiserum (obtained by inoculating a ferret directly with the human gargling), (*b*) A (PR8) ferret antiserum, and (*c*) B (Lee) ferret antiserum. After an hour's incubation at 37°C with homologous antiserum the virus, particularly the long forms, became almost completely agglutinated in large clusters, whereas in the presence of heterologous sera there remained many free rod forms together with some in relatively small groups. The diffraction from the filaments treated with antiserum was quite different from the normal control in that it was more diffuse and coloured and the surface

LEGENDS TO ILLUSTRATIONS ON PLATE

DR. CHU AND OTHERS: FILAMENTOUS FORMS ASSOCIATED WITH NEWLY ISOLATED INFLUENZA VIRUS

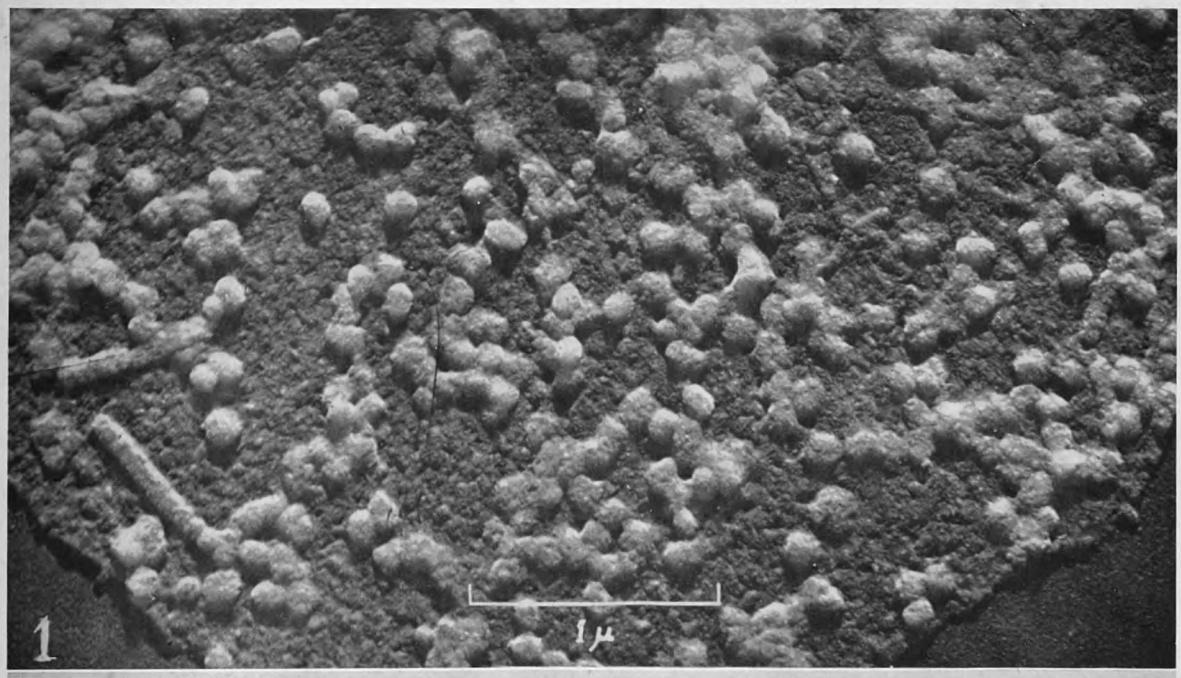
Fig. 1—Electron micrograph of influenza A (PR8) adsorbed on the membrane of the laked fowl red cell. Shadowed with palladium. The elementary virus bodies are generally round or ovoid, but elongated forms can be seen in the bottom left-hand corner.

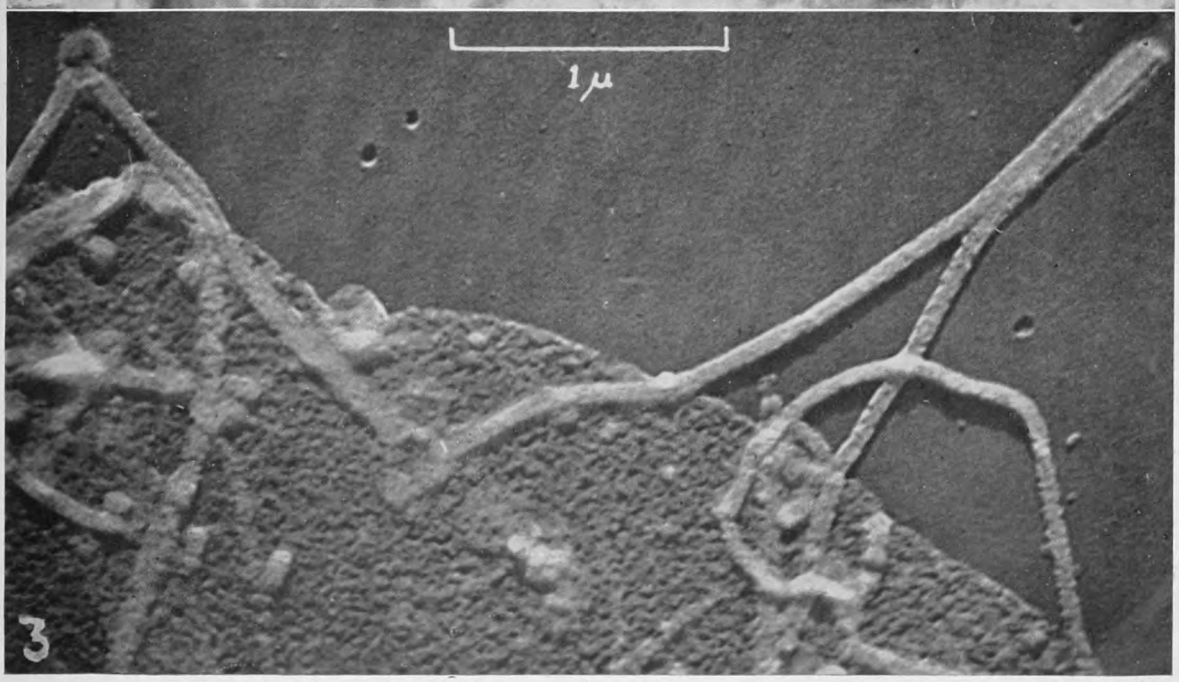
Fig. 2—Influenza A/Paris (PLI)/49 adsorbed from the allantoic fluid of the first egg passage. This electron micrograph is of unshadowed material by direct transmission. Note the variation in length and width of the filaments and the internal structure having intense absorption for electrons.

Fig. 3—Influenza A/Nederland I/49 adsorbed from allantoic fluid of the 4th egg passage. Palladium shadowed. This electron micrograph illustrates the exceptionally long filaments associated with these recently isolated influenza viruses.

Digitized by Google

DR. CHU AND OTHERS : FILAMENTOUS FORMS ASSOCIATED WITH NEWLY ISOLATED INFLUENZA VIRUS





Digitized by Google

DR. CHU AND OTHERS : FILAMENTOUS FORMS ASSOCIATED WITH NEWLY ISOLATED INFLUENZA VIRUS

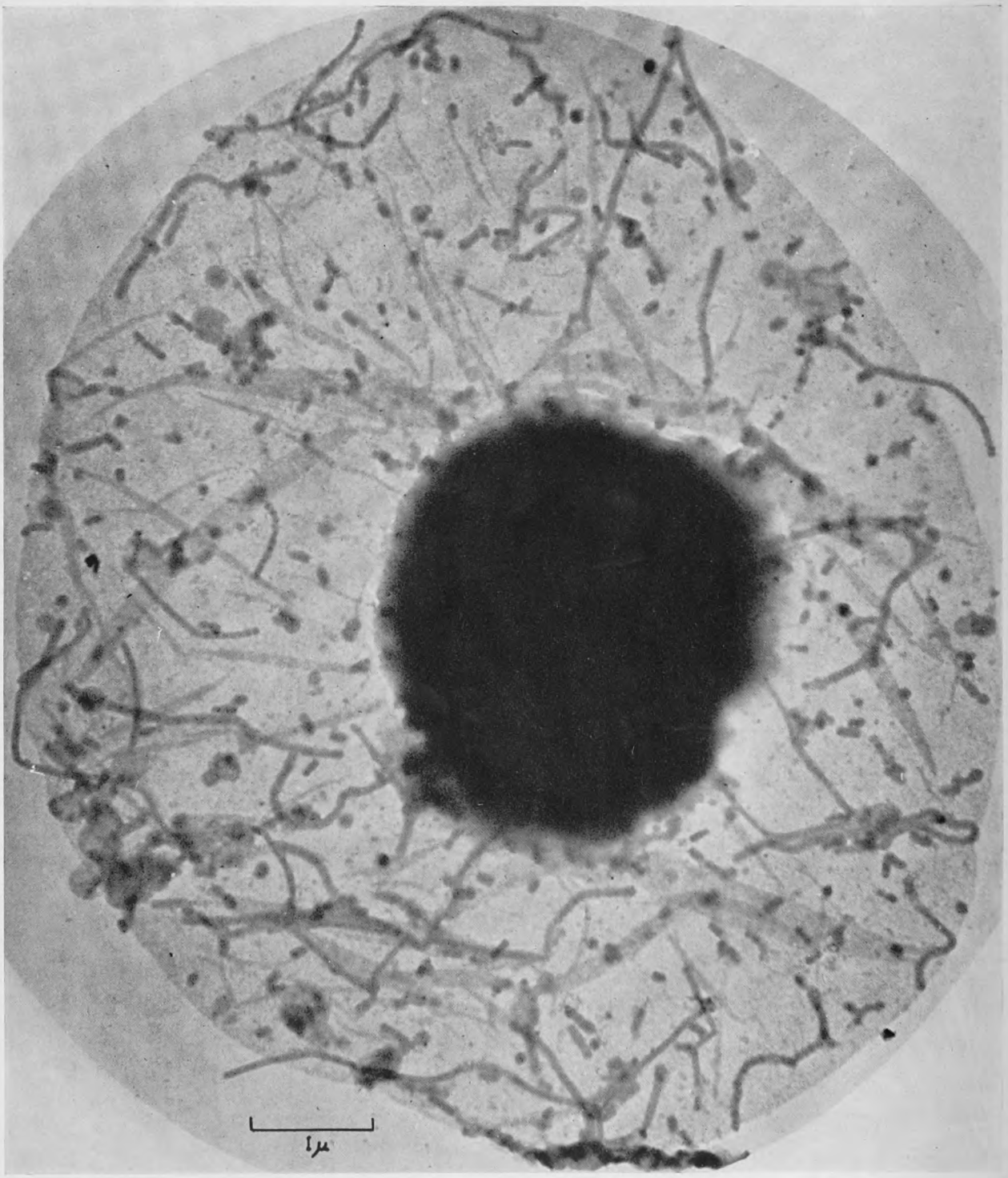


Fig. 4—Electron micrograph (by direct transmission) of virus of influenza A/Ocean Island/48 strain adsorbed on laked fowl red cell. The nucleus is surrounded by the delicate membrane, which is of double thickness, showing folds and creases. Both filamentous and round forms associated with the virus are seen. Note the variation in length of the filaments and the often beaded structure. The over-all picture is very similar to those obtained with Continental strains.

Digitized by Google

of the rods appeared roughened or beaded. This was presumably due to the superficial attachment of antibody or possibly particulate forms of virus.

(6) Two lines of egg passage with Nederland I virus have been maintained with (*a*) undiluted allantoic fluid and (*b*) 0·35 μ membrane filtrate. After the eight passages so far made both lines exhibit the long and the round forms. Allantoic fluid from eggs infected with the 1947 A strain, 'Barrett,' both mouse-adapted (11 passes) and unadapted (at least 15 passes in eggs), has been found to contain elongated forms in each instance, though in numbers and average length much less than observed with the recently isolated viruses. It is clearly a point of great interest and importance to know whether or not the morphological character of a virus, grown in a particular host, can alter on continued passage.

(7) The newly isolated influenza viruses have not yet been fully adapted to mice; but after one pass in mice or ferrets and then one pass in eggs the long forms were still observed. The presence of the filamentous forms in virus preparations of infected mouse-lung, or in tracheal washings from infected mice and nasal washings from ferrets, has not yet been convincingly demonstrated.

SEROLOGICAL AFFINITIES

Serological studies, to be reported later, show that the strains of virus A obtained in the recent outbreak are antigenically alike and closely related to, but not identical with, strains obtained in the U.S.A. and Europe in 1947. They are rather remotely related to the classical PR8 strain of A virus. They have been isolated in this laboratory or obtained from the following sources: Italy (Prof. B. Barbudieri, Rome, and Prof. E. Carlinfanti, Naples), Switzerland (Dr. J. Wirth, Geneva), France (Dr. Dujarric de la Rivière and Prof. P. Lépine, Paris), Holland (Prof. J. Mulder, Leiden), and England (Drs. J. A. Dudgeon, F. O. MacCallum, and A. P. Goffe). A virus apparently identical serologically and morphologically was recovered in October, 1948, from Ocean Island in the mid-Pacific and sent us by Dr. F. M. Burnet. Only further work will show if the appearances we describe are particularly well marked in these 1948–49 viruses, or if they are to be seen in all recently isolated strains. A few long forms were found in preparations of a B strain recently isolated in Czechoslovakia by Prof. D. Blaškovič but they were much less numerous than with the A viruses.

CONCLUSION

The evidence available suggests that these elongated filamentous structures seen in allantoic and amniotic fluids of eggs infected with recently isolated influenza virus represent a stage in virus multiplication. This view, should it be confirmed by more exhaustive studies, would revolutionise our conception of the way some viruses can multiply. Such dependence of virus form on the environment would constitute yet another point of resemblance between these viruses and some well-known micro-organisms. Further, it might obviously prove of practical importance in the preparation of vaccine.

We have recently discussed our findings with Prof. P. Lépine (Pasteur Institute) and Prof. B. Barbudieri (Rome), both of whom report having observed long forms of influenza strains recently isolated in their respective countries.

REFERENCES

Dawson, I. M., Elford, W. J. (1949a) *Nature, Lond.* **163**, 63.
— — (1949b) *J. gen. Microbiol.* (in the press).
Heinmets, F., Golub, O. J. (1948) *J. Bact.* **56**, 509.
Mosley, V. M., Wyckoff, R. W. G. (1946) *Nature, Lond.* **157**, 263.

RÔLE OF DI-ISOPROPYL FLUOROPHOSPHONATE IN SURGERY

J. P. QUILLIAM
M.B., M.Sc. Lond.
LECTURER IN PHYSIOLOGY, KING'S COLLEGE, LONDON

T. A. QUILLIAM
M.B. Lond.
LATELY RESIDENT ASSISTANT SURGEON, ST. CHARLES' HOSPITAL, LONDON

Di-isopropyl fluorophosphonate (D.F.P.) is a powerful anticholinesterase having an eserine-like action except that its combination with tissue cholinesterase seems to be irreversible. Its pharmacology and its clinical applications in myasthenia gravis and glaucoma have been reviewed by Quilliam.[1] Here we discuss its use in the postoperative syndromes of paralytic ileus, abdominal distension, and retention of urine. Our experience of D.F.P. as an agent to deflate the gastro-intestinal tract before operation for partial intestinal obstruction or before radiography, and its use in one case of megacolon, is also reported. In all 27 cases of various types, treated by us with D.F.P., are reviewed.

POSTOPERATIVE PARALYTIC ILEUS

We have previously reported[2] that D.F.P. showed considerable promise in the treatment of paralytic ileus, and this has been confirmed in America.[3] Since then we have extended our studies, though happily the skill of our surgical colleagues has somewhat restricted our experience of this condition. Our view that D.F.P. has a definite part to play in the treatment of paralytic ileus has been considerably strengthened, but we also think that it should by no means displace entirely such basic treatment as the relief of pain, sleeplessness, and anxiety, and the use of intravenous fluids and intragastric (or intestinal) suction, to which alone a fair proportion of cases respond. If these procedures do not arrest a deteriorating situation, then the use of D.F.P. may prove life-saving. The surgeon who operates must be prepared to institute and maintain any or all of the basic measures referred to above as the changing clinical picture may demand, calling upon D.F.P. as an additional measure when required.

Postoperative paralytic ileus may be defined as the inability of the patient to pass fæces or flatus within sixty hours of the end of an abdominal operation. The time of onset varies so that too rigid adherence to this definition may occasionally lead to withholding treatment in the prodromal period, often a particularly propitious time at which to start therapy, especially in cases in which suture or anastomosis of the gut has not been performed.

Three degrees of paralysis of the gut may be recognised after an abdominal operation:

(1) *Mild.*—Mild postoperative abdominal distension unaccompanied by clinical dehydration, in which the patient's general condition remains almost unaffected. This is quite common, and recovery from this state of "ileus," as it may be termed, is usually spontaneous on or after the third postoperative day. If this does not happen, the response to a single enema (once repeated if necessary) is speedy and copious.

(2) *Moderate.*—When the patient does not respond to such measures, the onset of paralytic ileus of moderate severity may be recognised. Bowel sounds are inaudible, and abdominal distension becomes severe (the patient being the most reliable guide to the degree of enlargement of his abdomen). Mild clinical dehydration appears after a short interval, and the patient's general condition begins to deteriorate. It is sometimes evident before the expiry of the sixty hours that paralytic ileus is inevitable; and, according to the probable cause of the condition and to whether or not the bowel has been anastomosed or sutured,

1. Quilliam, J. P. *Post-grad. med. J.* 1947, **23**, 280.
2. Quilliam, J. P., Quilliam, T. A. *Med. Pr.* 1947, **218**, 378.
3. Grob, D., Lilienthal, J. L. jun., Harvey, A. M. *Bull. Johns Hopk. Hosp.* 1947, **81**, 245.

Digitized by Google

treatment should be either palliative and expectant, for the time being at any rate, or early and vigorous.

(3) *Severe.*—Severe paralytic ileus is accompanied by all the signs referred to under (2) above; but, in addition, repeated vomiting is troublesome, and there is well-marked dehydration and a rapid deterioration in the general condition. The patient may resent intervention, but unremitting attention from medical and nursing staff alike is required. A combination of early supportive treatment for forty-eight hours or so after diagnosis, followed by stimulation of peristalsis, probably leads to the best results. Often the patient's desperate plight renders early supportive treatment little better than a temporary postponement of death; hence active measures are called for at once.

We tried to insist that in our cases the clinical diagnosis of paralytic ileus should be supported by the failure of two enemas, given within a few hours of one another, to produce any fæces; the following procedure was then instituted.

Procedure

The patient's general condition was carefully assessed. Unsuspected complications—e.g., impacted fæces, recurrent physical obstruction of the gut, and significant peritonitis—were excluded, and any necessary steps were taken to relieve pain, anxiety, and sleeplessness. Dehydration, if severe, was combated with intravenous fluid and plasma, and the exhaustion occasioned by repeated vomiting was relieved by intragastric suction. An "intake" and "output" chart was kept.

We have now adopted the following scheme for giving D.F.P., which should be modified to suit each patient's clinical needs. For example, debility, extremes of age, and emaciation are all indications for reducing the dosage. As soon as it is considered that the basic measures are not speedily relieving the paralytic ileus, we exhibit D.F.P. as follows.

We give 2–4 mg. of D.F.P. by intramuscular injection, dividing the dose equally between two sites to ensure speedy absorption. This is often followed within 2 to 3 hours by defæcation either spontaneously or in response to an enema. If not, the patient should be rested for 12–24 hours, if possible, before the same dose of D.F.P. is repeated. In almost every case this causes defæcation either spontaneously or after an enema. If the case is very urgent, a maximum of 2 mg. of D.F.P. may be given 4 hours after the first dose.

On some occasions the administration of D.F.P. (and a subsequent enema) may be followed only by the passage of flatus. This we consider sufficiently favourable to allow of a longer interval of rest between the two injections of D.F.P., for flatus may be the harbinger of fæces. Daily doses were not necessary when D.F.P. was used in this way.

We treat anxiety, pain, and insomnia, if troublesome, with non-opiates and reserve minimal doses of morphine for cases which do not respond to the simpler methods. In our series, 4 cases developed chest complications, thus no effort should be spared to preserve the pulmonary scavenging reflexes.

Results

We have successfully treated with D.F.P. 12 cases of paralytic ileus in adults. Two-thirds of the patients were men, and the oldest was aged 77. In 9 cases the paralytic ileus was severe, and in 3 moderately severe. The table summarises the salient features and gives the total dosage of D.F.P. used on each occasion.

Comment

Before 1947 we used posterior pituitary extract or 'Prostigmin' (neostigmine methylsulphate) or a combination of both when treating similar cases of paralytic ileus. Our clinical impression is that D.F.P. is more certain in its action than prostigmin, and on no occasion did it give rise to the unpleasant and sometimes dangerous side-effects which may attend the use of posterior pituitary extract. The beneficial effects of D.F.P. seem to last considerably longer than those of the other two drugs. On these grounds we consider D.F.P. superior to both posterior pituitary extract and prostigmin in paralytic ileus.

POSTOPERATIVE ABDOMINAL DISTENSION

This condition is distinguished from a mild degree of paralysis of the gut as defined above by the lateness of its onset and by the fact that passage of flatus or fæces has been noted on at least one postoperative occasion. In such cases where purgatives are ineffective

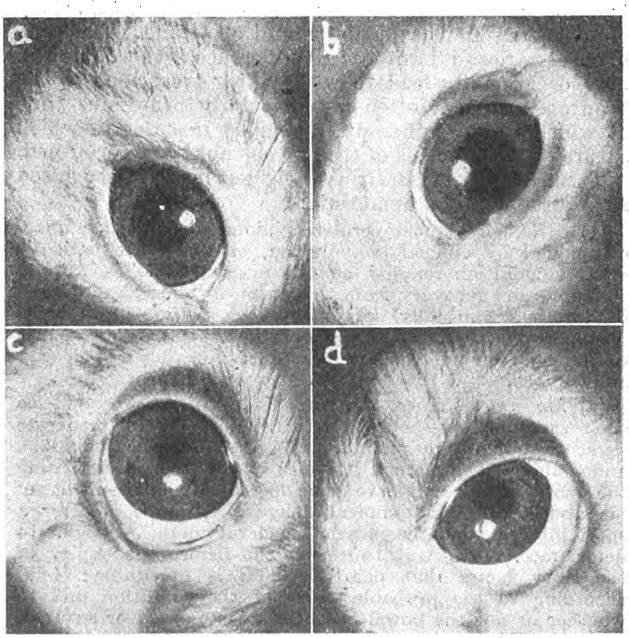


Fig. 1—Flashlight photographs of eyes of rabbit, showing sensitivity of miotic test to small variations in dosage of D.F.P.: *a*, untreated right eye; *b*, untreated left eye; *c*, right eye 72 min. after instillation of 5·5 μg. of D.F.P.; *d*, left eye 72 min. after instillation of 2·7 μg. of D.F.P.

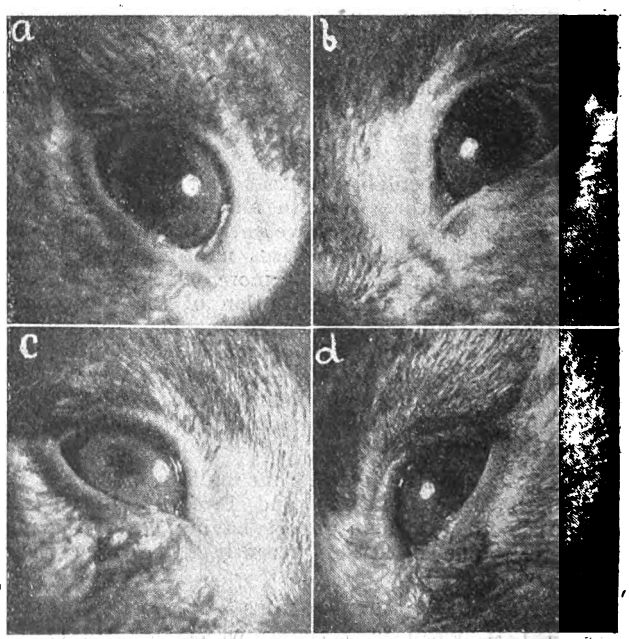


Fig. 2—Flashlight photographs of eyes of rabbit, showing that a sample of D.F.P. stored for two years had lost little, if any, potency: *a*, untreated right eye; *b*, untreated left eye; *c*, right eye 16 min. after instillation of 11 μg. of D.F.P. stored for two years; *d*, left eye 16 min. after instillation of 11 μg. of freshly dispensed D.F.P.

Digitized by Google

RESULTS IN POSTOPERATIVE PARALYTIC ILEUS

Case no.	Age (yr.)	Sex	Diagnosis at operation	Degree of paralytic ileus	Dosage of D.F.P.	Result
1	56	F	Obstruction from new growth of colon	Moderate	1 mg.	Paralytic ileus relieved
2	26	F	Perforated gastric ulcer	Severe	4 mg. in 20 hr.	,, *
3	31	M	Appendicitis and peritonitis	Moderate	2·5 mg.	,, *
4	64	F	Obstruction from omental band	Severe	1 mg.	,,
5	42	M	Obstruction from adhesions	Severe	7·5 mg. in 48 hr.	,,
6	46	F	Carcinoma of stomach (local resection)	Severe	2 mg.	,,
7	48	M	Perforated gastric ulcer	Severe	5·5 mg. in 24 hr.	,, †
8	47	M	Obstruction from internal hernia	Severe	4 mg. in 12 hr.	,, * ‡
9	71	M	Enlarged prostate (stage II prostatectomy)	Severe	8 mg. in 48 hr.	,,
10	41	M	Perforated gastric ulcer	Severe	2 mg.	,,
11	77	M	Right inguinal hernia (repair)	Severe	2·5 mg.	,,
12	45	M	Subdiaphragmatic abscess (drainage)	Moderate	2 mg.	,,

Cases 1–4 have previously been reported.[2]
* Developed pneumonia.
† Died of bronchopneumonia 8 days after operation.
‡ Recurrence of internal hernia caused death 7 days after operation.

and enemas contra-indicated, a "viscero-stimulatory" drug may be of great value. In 5 cases of this type D.F.P. was used successfully. The quantity of D.F.P. required was not more than 2·5 mg., a somewhat smaller amount than that usually necessary in paralytic ileus. Lasting relief was afforded to the patients without discomfort due to griping.

OTHER USES

Preoperative Preparation of Patients with Partial Intestinal Obstruction

D.F.P. has been used cautiously before operation to reinforce the effect of enemas with good results in 4 cases of subacute, partial, or chronic intestinal obstruction. Up to 13·5 mg. has been given in 72 hours to a patient aged 65. Smaller amounts were required for the other patients, the oldest of whom was aged 85.

In Radiography

D.F.P. was used in an attempt to promote the expulsion of fæces and gas from the alimentary tract before radiography. In 4 cases (largest dose 4·5 mg.) there was an evacuation of the bowel with evolution of flatus, but serial radiograms showed only a partial clearance of the abdominal field.

Retention of Urine

The administration of D.F.P. in several cases was followed by the voiding of urine. This suggested that it might prove useful in emptying a distended bladder in the absence of physical obstruction to outflow. In one such case occurring after operation, 4·5 mg. of D.F.P. initiated copious urination after a short time. We are trying to compare this action of D.F.P. with that of the other drugs now in common use for this purpose.

Megacolon

The vigorous stimulation of peristalsis seen in normal persons after as little as 1 mg. of D.F.P.[3] suggested the study of its action in megacolon. An emaciated child, aged 11 years, had received a four-pint barium enema, and most of this had been retained for 5 days. A total dosage of 5·5 mg. of D.F.P. given in 20 hours produced plenty of flatus but no fæces. Radiography showed that the retained barium had been passed to a more distal part of the bowel. In this case neither posterior pituitary extract nor prostigmin had any demonstrable action. The use of a spinal anæsthetic was considered inadvisable at the time. This was the only case in our series in which the D.F.P. produced transitory nausea. Otherwise we encountered no side-effects but if these are troublesome they may be readily controlled with atropine gr. $^1/_{75}$ (adult dose).

PREPARATION, ADMINISTRATION, STORAGE AND STANDARDISATION OF D.F.P.

For clinical use, it is convenient to dispense 0·5, 1, or 2 mg. of pure D.F.P. in glass ampoules containing 1 ml. of arachis oil. The oil is sterilised beforehand in the official manner by heating for an hour at 150°C. When cool, the appropriate amount of pure D.F.P. is added and the solution filled into sterile ampoules in 1 ml. quantities. The sealed ampoules are then subjected to final heating at 115°C. In cold weather this oil may not flow freely, and before use it may be necessary to warm the ampoule in the hand. Since D.F.P. is readily decomposed in the presence of traces of water, such as may be found in "absolute" alcohol, all syringes and needles used for giving it should be dry sterilised. Ampoules should be used immediately they are opened, since exposure to air causes some loss of potency.

The miotic activity of a sample of D.F.P. may be compared with that of an appropriate standard dilution of D.F.P. freshly dispensed, and this test provides a simple biological method of checking the potency of samples. A small measured volume of the sample to be tested is instilled into the right conjunctival sac of a rabbit, with a micro syringe. A similar volume of an appropriate standard D.F.P. dilution is placed in the left conjunctival sac of the same rabbit. A comparison of the mean pupil diameters under constant conditions of illumination made at 10-min. intervals during the hour following administration will indicate whether the sample under test is more or less potent than, or equipotent with, the standard. By adjusting the dosage of the stored sample it is possible to assess any loss in its potency.

In one biological test a sample of D.F.P. dispensed in arachis oil and stored for two years at room temperature was compared with a freshly made standard solution. It was impossible to detect any material loss in potency of the stored specimen. In other tests little, if any, loss in potency has been found with various periods of storage up to two years. In the interests of accuracy at least six rabbits should be used for each comparison, and a "cross-over" test made with the same group of rabbits a week later.

Figs. 1 and 2 illustrate the type of results obtained with this test.

SUMMARY

The use of D.F.P. in postoperative paralytic ileus is illustrated in 12 successfully treated cases. The drug should be used as a supplement to other measures.

Digitized by Google

D.F.P. was thought to be more powerful, more reliable, and more sustained in its action than prostigmin, and it did not give rise to the unpleasant side-effects occasionally encountered with posterior pituitary extract.

D.F.P. was used successfully in 5 cases of postoperative abdominal distension and 4 cases of intestinal obstruction, and in postoperative retention of urine. In megacolon and for removing flatus from the abdominal field before radiography good results were not obtained.

A simple biological test to assess the potency of a given sample of D.F.P. is described. This test showed that there was little, if any, loss in potency of the D.F.P. dissolved in arachis oil after storage for up to two years at room temperature.

We wish to thank our surgical colleagues who rendered this study possible; the doctors, nurses, and medical auxiliaries at the hospitals concerned; Dr. A. R. C. Butson for making photographs of the results of the biological test described, and Mr. F. H. Newman, PH.C., for dispensing the D.F.P.

OPERATION FOR SEVERE VARICOSE VEINS DURING PREGNANCY

HAROLD DODD
Ch.M. Lpool, F.R.C.S.
SURGEON, ROYAL HOSPITAL, RICHMOND; KING GEORGE HOSPITAL, ILFORD; ROYAL LONDON HOMŒOPATHIC HOSPITAL; AND PRINCESS LOUISE HOSPITAL, KENSINGTON

VARICOSE veins are an additional burden for many women during and after their pregnancies. Childbearing may be made miserable by the sleeplessness, pain, itching, weight, and swelling caused by enlarged veins in the legs, at the anus, and in the lower abdomen. Occasionally these varicosities are only temporary, but generally some persist after parturition and are aggravated by subsequent pregnancies and in middle age. Sometimes the discomfort and disability are so great that women, either on their own initiative or on medical advice, desist from bearing further children.

Since 1931 about which time surgeons began to use simultaneous ligature and injection for varicose veins, reports of operations on varicose veins in pregnancy have been scanty, but all the writers tell of success with injections.

Nicholas (1936), reporting his treatment of 100 gravid women by injection with 50% dextrose and 30% sodium chloride, points out that it reduces thrombophlebitis in the legs after delivery and gives great comfort during pregnancy.

McCausland (1939), reporting on 150 patients treated by injection in any month of pregnancy, obtained good results. He says that the danger of bleeding from ruptured varices is minimised by treatment.

Barber (1929) described excellent results from injection.

Selomons (1937) also relates satisfactory injections of varicosities in pregnancy. He advises against it in the presence of uncompensated heart lesions or high blood-pressure. He used quinine and urethane in doses of 2 ml. He found reports of 2 cases of uterine hæmorrhage and one of premature delivery after this. Of 45 cases followed up all were improved and two-thirds were "charmed." In only 3 had varicose veins recurred. The puerperium was normal.

Verovitz (1940) writes about his success with injections recommending 2% sodium recinoleate.

Cheatham and Peck (1936) treated 46 patients in a series of 838 pregnant women by injection of sodium morrhuate to within a fortnight of delivery.

Ochsner and Mahorner (1937) say that of 247 people seen with varicose veins 60% were pregnant. They recommended ligation if the valves of the internal saphenous vein were incompetent. If the valves were sound, injections were given and these were followed by 57% recurrence, whereas ligation of the internal saphenous vein in several places with simultaneous injections of sclerosing fluid was followed by only 18% recurrence.

Siegler (1939) says that operation is contra-indicated. He injected a mixture of equal parts of glucose 50% and sodium chloride 30% in doses of 10 ml.

Vignes (1939) advised rest in bed and injections as a last resort. He mentions 1 patient operated on with good results.

Slamova (1939) thinks that injections of glucose and salt at intervals of 3–6 days are good.

Edwards (1935) says that during pregnancy treatment is desirable and safe, provided oxytocic substances, such as quinine, are avoided. Sodium morrhuate is the solution of choice.

Greene (1932) finds that the danger of quinine injections in pregnancy has been exaggerated, as witness the large doses given for the treatment of malaria in the tropics. It is unwise to postpone treatment until after confinement. He treated 25 cases with weekly injections of quinine-urethane solution. No miscarriage occurred.

McPheeters (1931, 1934) reports that some of his most gratifying results have been obtained in the treatment of varicose veins during pregnancy.

Against these generally favourable reports must be set the opinion of a number of authorities (personal communications) who avoid active interference during pregnancy. As one of them wrote to me: "I recommend the patient to keep at least ten miles away from any surgeon who shows signs of using a scalpel."

RESULTS IN SEVENTEEN CASES

My experience is that varicose veins in pregnancy can be cured. This opinion is based on a follow-up of those who have had their veins operated on in or between pregnancy and have since passed uneventfully to full term. The possible exception is those women who have had white leg, but fortunately these are rare, and for them some relief can be given for the associated varices, œdema, eczema, and ulcers of the leg by supporting adhesive bandages or elastic stockings.

I have performed ligature and injection of varicose veins on 17 pregnant women, the first in 1942. The operations have been carried out between the second and seventh months of pregnancy. All these patients have been improved, and neither mother nor child has shown any ill effects. The babies have been born uneventfully, and the discomfort of the veins has been relieved.

In all the women the veins were varicose before conception and were made much worse by the growing fœtus. The diagnosis was obvious on inspection, and there was an impulse palpable in the varicosities when the patients coughed. The Trendelenburg tourniquet test was positive in all. In one case the external saphenous vein was incompetent, but in the others the internal saphenous vein was the defective vessel. Fortunately none had a history of white leg. In 15 women one leg was affected, and in the other 2 both limbs were concerned.

The first woman was treated in 1942, when she was seven months pregnant. She was incapacitated and unable to attend to her young family of four; her husband was on war service. She had varicosities on the abdomen and left thigh and leg. At the operation the bleeding from the superficial dilated fragile venules was considerable. A good result followed. This first case was the most difficult.

Since then, all pregnant women presenting with gross troublesome varicose veins have been operated on, or injections have been made in other veins which were not so tiresome. Another factor in favour of immediate radical treatment is that not only does it give continuous relief but also it may prevent phlebitis after childbirth. Again, though the veins subside somewhat after parturition, those present before conception often persist to an increased extent and cause subsequent trouble, unsightliness, and, in some women, inferiority feelings. It may be better for the treatment to be given before the baby is born than afterwards when continuous nursing is needed.

Digitized by Google

DIAGNOSIS

Superficial enlarged veins in the legs may be either varicose or compensatory to blocked deep veins. Compensatory enlargement must be differentiated from varicose veins, because these compensatory veins must not usually be treated by occlusive therapy. Fortunately they are very rare. To test the patency of deep veins, rubber bands are applied round the middle of the thigh and leg, tight enough to compress the subcutaneous vessels but not the deeper ones. The patient walks or climbs stairs for 3 minutes. If the venæ comites are obstructed, the blood must return chiefly through the superficial veins, which being obstructed by the constricting bands distend and cause great pain, making the patient beg for release. If the exercise is performed fairly comfortably, the intramuscular vessels are patent, for the blood is returning through them; therefore the superficial dilated vessels are varicose.

Types of Varicose Veins.—The diagnosis of the type of varicose lesion is essential for planning the operation; there are at least seven:

(1) Incompetence of the internal saphenous vein.
(2) „ „ „ external „ „
(3) „ „ „ internal and external saphenous systems together.
(4) „ „ „ communicating veins of the leg and/or the thigh.
(5) „ „ „ internal saphenous system and a communicating vein.
(6) „ „ „ external saphenous system and a communicating vein.
(7) „ „ „ internal and external saphenous systems and a communicating vein or veins.

These types are principally indicated by a positive Trendelenburg tourniquet test and differentiated by variations according to the type present (Dodd 1947). With severe varicose veins an impulse or a thrill is palpable in the varices when the patient coughs. The enlarged vessel may be palpable in the groin or a saphena varix visible.

OPERATION

Indications.—When one of these types is clearly present, operation is required, because injections, even when heroic, have been followed by recanalisation in from three months to three years, not to mention the possibly harmful constitutional reactions provoked by the various sclerosants.

The procedure can be done safely up to seven months, but after this the general pressure of the enlarged uterus makes the operation difficult by causing bleeding from fragile venules, and labour might be precipitated by the anæsthetic and by surgical trauma. After seven months it is better to bandage the legs from the ankle to the groin, and for patients to take considerable rest. The indications for the operation are that the veins had given trouble before conception and were considerably aggravated by the pregnancy.

The contra-indications are constitutional illness, vomiting, albuminuria, and pyelitis of pregnancy, and any condition which would veto a clean operation, moderate in extent.

The *anæsthetic* and the other drugs used during the operation are selected to avoid stimulating the uterus or harming the child. Either a local analgesic or a skilfully given general agent is selected. All the operations in this series were done under general anæsthesia with gas, oxygen, and a little ether.

The *operation* is performed with aseptic technique in a major theatre, where full surgical assistance is available for there may be torrential hæmorrhage from a varix torn during the ligation. It requires about 20 minutes and occasionally up to an hour.

The procedure (Dodd 1944) consists in ligature and division of the internal saphenous vein at its union with the common femoral vein, and division of all the associated branches, which vary from two to ten in number.

A long needle with a rough olive-shaped head is inserted down the great saphenous vein from the groin and 30 ml. of 20% common salt solution or 10 ml. of a solution of phenol crystals 2%, glycerin 30%, glucose 30%, and autoclaved gelatin 1/4% (called P3G) is injected slowly as the needle is withdrawn. The purpose of the abrasive needle-tip is to denude the venous endothelium and thereby to ensure a firm thrombosis followed by organisation and permanent occlusion; recanalisation—i.e., recurrence—of the vein is therefore unlikely. The mechanical scarification is carried out by pressing with the fingers on the skin over the head of the needle, which is moved up and down in short strokes throughout the length of the vein it has traversed. The grating is easily felt, and clotting follows, even without the sclerosing fluid, some of which also escapes into some of the subcutaneous varices and thromboses them.

The internal saphenous vein is exposed at the ankle, and a further 20 ml. of 20% saline solution or 10 ml. of P3G solution is injected upwards through a catheter or a smaller rough-headed long needle. The operation is done with meticulous asepsis, precision, and gentleness.

Occasionally the external saphenous vein in the popliteal space must be dealt with. This occurred once in this series of 17 women. Sometimes the communicating veins in the lower thigh and lower half of the leg must be located and tied; but this is uncommon, because the procedures described on the saphena magna and short saphenous vein generally render the communicating veins ineffective.

The injection fluid is important. Locally it must be a powerful sclerosant, but it must be harmless to the deep veins and constitutionally benign to the patient and to the baby. It must not cause the pregnant uterus to abort. For this reason I consider that sodium morrhuate, quinine and urethane, salicylates, and 'Ethamolin,' which have caused illness and deaths in non-pregnant women, are unsuitable. I think that the safe agents are common salt 20% solution, saturated glucose 60% solution; and the P3G fluid, which I have used with good results and no ill effects over two thousand times. On non-pregnant patients it is very promising and has been injected seven times at operation on pregnant women with good effect.

The patients get up the day of, or after, the operation and thereafter daily for increasing periods. They are encouraged to exercise.

CONCLUSIONS

The consensus of opinion seems to be that the treatment of troublesome varicose veins in pregnancy is permissible and justifiable. Injections give some relief. I have ventured a step further by adopting operation, and report success in 17 pregnant women with gross and troublesome varicose veins so treated. I make a plea that incapacitating and painful varicose veins during gestation be treated by ligature and injection.

REFERENCES

Barber, T. F. T. (1929) The Treatment of Varicose Veins of the Lower Extremities by Injections. New York.
Cheatham, G. R., Peck, A. E. (1936) *N.Y. St. J. Med.* **36**, 1871.
Dodd, H. (1944) *Brit. med. J.* ii, 814.
— (1947) *Post-grad. med. J.* **23**, 427.
Edwards, E. A. (1935) *J. Amer. med. Ass.* **104**, 2077.
Greene, R. (1932) *J. Obstet. Gynæc.* **39**, 601.
McCausland, A. M. (1939) *West. J. Surg.* **47**, 81; *Calif. West Med.* **50**, 258.
McPheeters, H. O. (1931) *J. Lancet*, **51**, 589; *Trans. Sect. Obstet. Gynec. abdom. Surg. Amer. med. Ass.*, p. 136.
— (1934) *Minn. Med.* **17**, 33.
Nicholas, C. Z. (1936) *Amer. J. Obstet. Gynec.* **31**, 476.
Ochsner, A., Mahorner, H. (1937) *Surgery*, **2**, 889.
Siegler, J. (1939) *Amer. J. Surg.* **44**, 403.
Slamova, B. (1939) *Cas Lék. ces.* **78**, 369.
Solomons, E. B. (1937) *J. Obstet. Gynæc.* **44**, 650.
Verovitz, C. H. (1940) *J. Amer. Inst. Homœop.* **33**, 71.
Vignes, H. (1939) *Rev. gén. Clin.* **53**, 131.

Digitized by Google

MORTALITY FROM PINK DISEASE IN 1923-47

WILLIAM P. D. LOGAN
M.D., B.Sc. Glasg., D.P.H.
From the General Register Office

INTEREST in this relatively rare and ætiologically obscure disease of childhood has been stimulated by the suggestion of Warkany and Hubbard [1] that mercury administered in teething powders or in ointments may be the causal agent; out of 20 cases of pink disease mercury was found in the urine of 18. It may be opportune, therefore, to review the mortality of pink disease in England and Wales during the past twenty-five years.

The synonyms for pink disease include erythrœdema, erythrœdema polyneuritica, dermato-polyneuritis, and acrodynia, but their use on death certificates is being steadily given up in favour of the simpler name.

Table I gives the number of deaths and the death-rate from pink disease in each year from 1923 to 1947, and fig. 1 illustrates the trend of the death-rate over those years.

Starting with 1 death in 1923 (a rate of 0·3 per million) the recorded deaths and the death-rate progressively increased, as the disease became more widely recognised, up to 1936, when there were 88 deaths (31·4 per million). For the next three years the numbers fluctuated, dropped to a much lower level in 1940 (49 deaths, 17·0 per million), and remained practically constant at this lower level during the next six years. It is difficult to believe that this was a chance sequence, and it cannot be explained by changes in the birth-rate, which behaved dissimilarly. In 1947, however, deaths rose sharply; the number (103) was the highest yet recorded, and the death-rate (29·2 per million) was almost as high as in 1936. The figures, it should be noted, have not been corrected for the changes in classification that came into force in 1940. But application of the appropriate conversion factor would only partially reduce the drop in 1940 and would not materially alter the picture.

The association here revealed between the mortality of pink disease and the war may or may not indicate a real temporary change in the behaviour of the disease. The circumstances of war may have altered the standard of death certification of pink disease; or may have reduced its prevalence or fatality.

As table I shows, variations in the predominating sex occurred randomly from year to year. In numbers of deaths each sex predominated in twelve of the twenty-five years, whereas in 1945 the deaths were divided equally between the sexes. The female death-rate exceeded the male in thirteen years. Table II shows that, aggregating years 1923–47, there was no significant difference between the sexes: 49·2% of deaths in males, and 50·8% in females. The percentage for each sex differs from expectation (the 25-year average proportion of each sex in the child population: males 50·8% and females 49·2%) by 1·6%, with a standard error of 1·5%.

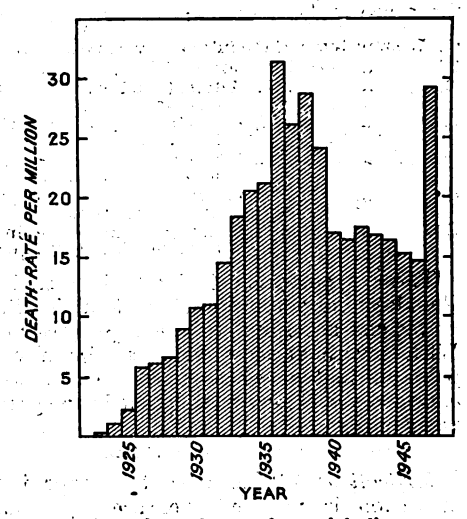


Fig. 1—Annual death-rates from pink disease per million children under 5 years of age in England and Wales in 1923-47.

Most deaths occurred under the age of 1 year, and none over the age of 9 years. In four of the earlier years (1923, 1924, 1928, and 1932) deaths at ages over 1 year were more numerous than those under 1 year; but after 1932 the lowest age-group has persistently shown an excess ranging from 7 to 32, except in 1940, when the excess was only 1 death.

Table II shows that, of all the deaths in 1923–47, about 61% were in children under 1 year, 38% at

1. Warkany, J., Hubbard, D. M. *Lancet*, 1948, i, 829.

TABLE I—ANNUAL DEATHS BY SEX AND AGE, AND ANNUAL DEATH-RATES (ALL AGES), PER MILLION CHILDREN AGED UNDER 5 YEARS, IN ENGLAND AND WALES IN 1923–47

Years	Annual deaths								Annual death-rate*		
	Male				Female			Both sexes (all ages)	All ages		
	Age (yr.)			All ages	Age (yr.)			All ages			
	0–	1–	5–		0–	1–	5–		Male	Female	Both sexes
1923	..	..	..	..	..	1	..	1	1	..	0·6	0·3
1924	..	1	..	1	..	3	..	3	4	0·5	1·6	1·1
1925	3	..	..	3	1	4	..	5	8	1·7	2·9	2·3
1926	6	4	1	11	5	4	..	9	20	6·4	5·4	5·9
1927	3	3	..	6	8	6	..	14	20	3·6	8·6	6·1
1928	5	8	..	13	4	4	..	8	21	8·1	5·1	6·6
1929	11	5	..	16	8	4	..	12	28	10·2	7·8	9·0
1930	14	5	..	19	8	6	..	14	33	12·3	9·3	10·8
1931	7	6	1	14	13	6	..	19	33	9·2	12·8	11·0
1932	15	10	2	27	5	11	..	16	43	18·0	10·9	14·5
1933	18	11	..	29	14	11	..	25	54	19·5	17·3	18·4
1934	23	10	..	33	18	8	..	26	59	22·6	18·3	20·5
1935	21	13	..	34	18	7	1	26	60	23·6	18·6	21·2
1936	23	14	..	37	24	26	1	51	88	26·0	37·0	31·4
1937	15	11	..	26	28	19	..	47	73	18·3	34·3	26·1
1938	24	18	..	42	24	15	..	39	81	29·3	28·2	28·7
1939	18	9	..	27	24	16	2	42	69	18·5	29·9	24·1
1940	12	11	..	23	13	13	..	26	49	15·7	18·4	17·0
1941	16	6	..	22	12	13	..	25	47	15·2	17·9	16·5
1942	18	10	..	28	12	10	..	22	50	19·2	15·7	17·5
1943	17	3	..	20	18	11	..	29	49	13·4	20·3	16·8
1944	17	11	..	28	15	7	..	22	50	18·2	14·9	16·5
1945	15	8	1	24	16	8	..	24	48	15·0	15·7	15·3
1946	13	6	..	19	22	7	..	29	48	11·4	18·3	14·7
1947	43	15	..	58	32	13	..	45	103	32·0	26·1	29·1

* Though 9 deaths are included at ages 5–10, these death-rates were calculated on the basis of the 0–5 age-group populations, a course which was considered more appropriate here than to exclude the 9 deaths or to base the rates on the 0–10 age-group populations.

TABLE II—DISTRIBUTION OF DEATHS IN ENGLAND AND WALES IN 1923–47, BY SEX AND AGE

Age (yr.)	Male	Female	Both sexes
0– ..	357	342	699 (*61·4%*)
1– ..	198	233	431 (*37·8%*)
5– ..	5	4	9 (*0·8%*)
All ages ..	560 (*49·2%*)	579 (*50·8%*)	1139 (*100%*)

Digitized by Google

TABLE III—DEATHS (FOR COMBINED SEXES) AT AGES UNDER 1 YEAR AND UNDER 5 YEARS IN ENGLAND AND WALES, 1940–46

(*a*) Under 1 year

Age	Under 4 weeks	4 weeks to 3 months	3–6 months	6–12 months	Total under 1 yr.
No. of deaths ..	2	4	26	184	216
Per cent. of total	0·9%	1·9%	12·0%	85·2%	100%

(*b*) Under 5 years

Age (yr.)	0–	1–	2–	3–	4–	Total under 5 yr.
No. of deaths ..	216	113	8	3	Nil	340
Per cent. of total	63·5%	33·2%	2·4%	0·9%	Nil	100%

ages 1–4 years, and less than 1% at 5 years of age or over. There was no significant difference in age-distribution between the sexes ($\chi^2 = 2{\cdot}63$, $P > 10\%$). For the years 1940–46 table III provides a further analysis of deaths by age: 63·5% of all deaths under 5 years were in children aged under 1 year, and 33·2% between 1 and 2 years. Among deaths under 1 year over 85% took place in the second 6 months of life. There were few deaths under 6 months or over 2 years of age.

Discussing the age-distribution of morbidity in pink disease, Fisher,[2] who had formed the impression that with the passage of time the "age of attack" was becoming lower, found, on analysis of his figures, no evidence of any significant age-shift. In our present series of deaths, on the other hand, there is evidence of a significant age-shift between 1923 and 1947 from the higher to the lowest age-group. (By Spearman's rank correlation technique, $\rho = 0{\cdot}63$, significant by Student's *t* test at a level of between 0·1%.)

The deaths, aggregated for the years 1940–46, in each of the twelve main regions of England and Wales are contained in table IV. In the absence of information about regional populations at ages during the war years, total live births in each region, aggregated for the same years, have been used as a base for the calculation of "death-rates." Such rates, it should be noted, do not take account of migrational movements of the child population during the war.

There are highly significant differences between the rates in the twelve regions ($\chi^2 = 117{\cdot}89$. $P < 0{\cdot}0001\%$). The highest rate was recorded in North I (201·4 per million), followed by Wales II (158·7) and North III (114·3). The lowest rate occurred in the South-west region (24·1), followed by the South-east (38·3), and then by Greater London (40·9). These regional differences are illustrated, and may be compared region with region, in fig. 2.

The regional distribution of deaths in 1947 is shown in the last column of table III. It will be seen that the large increase in deaths during that year was not concentrated in any one part of the country but was shared among the regions in about the same proportions as in previous years.

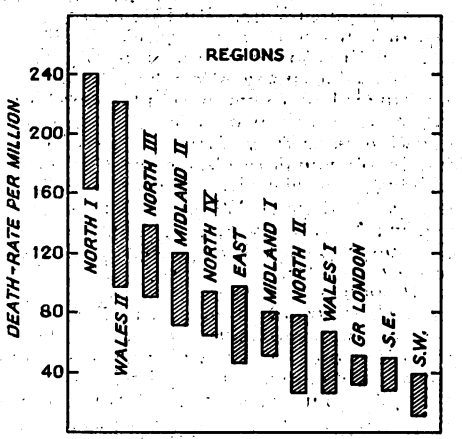


Fig. 2—Regional death-rates from pink disease per million live births in 1940–46, with abbreviated confidence intervals to test whether differences are 5% significant.

Method of Construction

The abbreviated confidence interval technique has been devised by a statistician of the General Register Office. The abbreviated intervals are obtained by reducing, in the proportion $1 : \sqrt{2}$, the confidence intervals of Neyman.

The diagram provides a useful approximation to the results that would be obtained by carrying out 66 tests of significance to compare each possible pair of regions. Before using this technique it is essential, as has been done here, first to establish a significant general heterogeneity of the regions by means of a χ^2 or other equivalent test.

Method of Use

Note whether the rectangles representing any chosen pair of regions overlap on the vertical scale. If they overlap—e.g., North III and East—there is no significant difference between the two regions. If they do not overlap—e.g., North III and Midland I—there is a significant difference between them.

A significant difference can be taken as one which is more than twice its standard error, and this criterion of significance was adopted in constructing the diagram.

It is conjectural whether these differences in death-rate between the regions are due to differences in morbidity, in fatality, or in standards of diagnosis. It would be interesting to know whether there exist regional differences of habit in the administration of mercurial medicaments to young children.

SUMMARY

The death-rate of pink disease fell to a constant low level during the late war but rose sharply in 1947.

There was no significant difference in sex-mortality over the years 1923–47.

About two-thirds of the deaths were in children aged under 1 year, especially at ages 6–12 months. Of the other third practically all were between the age of 1 and 2 years.

During 1940–46 there were highly significant differences between regional death-rates.

2. Fisher, T. N. *Brit. med. J.* 1947, 1, 251.

TABLE IV—REGIONAL DISTRIBUTION OF DEATHS IN 1940–46 AND IN 1947, AND REGIONAL DEATH-RATES PER MILLION LIVE BIRTHS IN 1940–46, IN ENGLAND AND WALES

Region*	Number of deaths, 1940–46							Death-rate (per million live births), 1940–46, both sexes, all ages	No. of deaths (both sexes, all ages), 1947
	Male Age (yr.)			Female Age (yr.)			Both sexes (all ages)		
	0–	1–	5–	0–	1–	5–			
Greater London ..	7	7	..	9	11	..	34	40·9 ± 7·0	5
Remainder of S.E.	4	11	..	6	5	..	26	38·3 ± 7·5	8
North I	20	4	..	18	12	..	54	201·4 ± 27·4	10
North II	3	..	..	2	3	..	8	51·2 ± 18·1	4
North III	15	8	..	18	5	..	46	114·3 ± 16·9	14
North IV	18	12	1	16	9	..	56	78·8 ± 10·5	22
Midland I	19	4	..	8	11	..	42	65·8 ± 10·2	17
Midland II	10	5	..	14	1	..	30	95·5 ± 17·4	7
East	7	1	..	6	2	..	16	71·4 ± 17·9	3
South-west	..	..	..	2	4	..	6	24·1 ± 9·8	7
Wales I	2	1	..	6	1	..	10	45·6 ± 14·4	5
Wales II	3	2	..	3	5	..	13	158·7 ± 44·0	1
England and Wales	108	55	1	108	69	..	341	71·4 ± 3·9	103

* For the geographical constitution of the regions, see the Registrar-General's Statistical Review (any recent year).

Digitized by Google

Medical Societies

ROYAL SOCIETY OF MEDICINE

Carcinoma of the Breast

AT a meeting of the section of surgery of the Royal Society of Medicine on March 23, with Mr. JULIAN TAYLOR, the president, in the chair, a paper on Surgery, Irradiation, and Hormones in Breast Cancer was read by Prof. FRANK E. ADAIR (New York).

Dr. Adair said that at the Memorial Hospital he had had experience of altogether 13,000 cases of breast cancer, including 8000 which were operable and 125 cases in men. His present survey was based on 3988 cases studied since 1935. The method was to apply a certain line of treatment in a series of cases, and at the same time to run a parallel control series treated by surgery alone; the experimental line of treatment was changed from time to time. By this means it had been possible to obtain comparable figures for the results of treatment, and thus to draw certain definite conclusions. In one series radiotherapy alone had been used. This form of treatment had an honoured place in the palliation of inoperable cases, but as a method of cure it was only half as effective as surgery alone. In two parallel series with gland involvement treated respectively by X rays and by surgery, the five-year cures were 26% and 50%. The usual dose had been 3000 r. Admittedly this dose was not large; viable cancer cells might be found after the application of as much as 3600 r, and 5000–6000 r was necessary to ensure the total destruction of the neoplasm though such doses seriously damaged the normal tissues, especially bone, skin, and lungs. One striking effect of irradiation of the axilla was the "spotty" action on the involved glands; in one gland there might be complete destruction of cancer cells, while in another immediately adjacent there was no effect at all.

Radical operation was combined with preoperative irradiation in a series of cases between 1934 and 1940. The diagnosis was confirmed by aspiration biopsy, and X rays were applied in a dose of between 1200 and 3600 r per portal. Mastectomy was done after an interval of from one to six months, depending on the amount of skin reaction. Healing was poor after the larger X-ray doses. The five-year results in cases of cancer confined to the breast showed cure in 74·9% as opposed to 82·2% in those treated by surgery alone. When the axilla was involved, the corresponding figures were 40% and 43%. Dr. Adair believed that these results were the death knell of preoperative irradiation; for him the issue was settled. It was probably the inevitable delay in operation which mainly caused the poor results of preoperative X-ray therapy.

Since 1940 immediate radical mastectomy without any irradiation had been his standard treatment for cases in which the cancer was confined to the breast. A postoperative course of X rays was given if the axilla was involved, and he thought that the rate of cure was raised by between 3 and 5% by the irradiation. At the same time postoperative X rays increased the risk of œdema of the arm. This scheme of treatment had produced encouraging results.

The hormone treatment of breast cancer rested on a basis of experimental work in which British investigators had played a leading part. In America an extensive clinical trial had been organised and its results were shortly to be collated. In this lecture Dr. Adair was concerned only with the results obtained at the Memorial Hospital. Here he was director of a team which included, besides doctors, a steroid chemist, a nurse, and a social worker. They used mostly androgens and favoured particularly testosterone propionate. At first they had given 25 mg. a day, but more recently they had been trying as much as 200 mg. a day with better results. In addition to the advanced cases treated only by hormones, Dr. Adair had implanted 300 mg. of testosterone propionate at operation in each of 500 cases of radical mastectomy, and most of these had amenorrhœa for six months. Their experience of œstrogens had been smaller and the results less impressive than with the androgens, but he thought that perhaps the dosage (100 mg. stilbœstrol three times a week) had been rather small, for Nathanson, who used much larger doses (200 mg. a day) claimed much better results. It might be that œstrogens yielded their results more slowly than androgens.

On the whole the results of hormone treatment were encouraging, particularly in relieving symptoms. Malaise and dyspnœa were relieved in 85% of cases, and pain in 75%. There was also objective improvement and evidence of regression of secondaries, particularly in liver and bones, and an average increase in hæmoglobin of 26%. The side-effects of hormone treatment were important and sometimes troublesome. Œdema and increase in weight were caused by both androgens and œstrogens. Œstrogens caused nausea in a quarter of the cases, and quite troublesome uterine hæmorrhage in some postmenopausal women. Sometimes testosterone therapy caused a severe shock-like condition, due to its powerful effect on calcium metabolism. Secondaries in bone were associated with a rise in the blood-calcium, and the administration of testosterone brought the level back to normal by causing the reposition of calcium in bone; this process of bone repair was also signalised by a rise in the alkaline phosphatase. Histological studies of the effect of hormones on breast cancer showed an almost identical picture with the effect of X rays—principally nuclear disintegration and voluminous fibrosis.

There sometimes came a time during treatment with androgens when the patient not only ceased to improve but became much worse. If the hormone treatment were now stopped altogether, or œstrogens substituted for the androgens, great improvement might take place. Dr. Adair illustrated this effect with the account of a striking case of a woman who developed crippling bony secondaries several years after starting treatment with testosterone, and who improved so greatly after the hormone was discontinued that twenty-two months later she was doing her own housework. This effect was not clearly understood but was thought to be due to the adaptation of the body to its artificial hormonal environment.

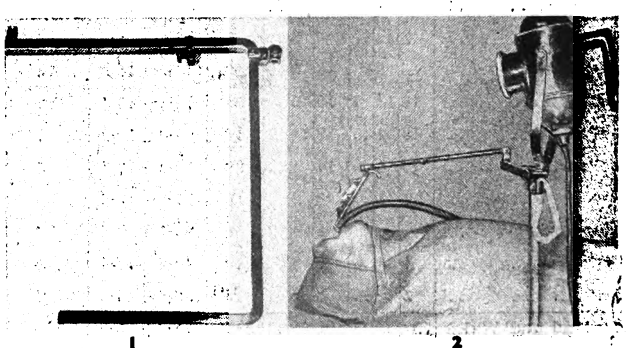
Dr. Adair thought that the present achievements of hormone therapy gave much hope for the future, and that one of the most promising lines of advance lay with the chemists, who would synthesise new preparations of greater power and selectivity.

New Inventions

SUSPENSION BAR FOR THE DAVIS GAG

THIS simple suspension apparatus for the Davis gag consists of a stout steel bar, square on section and bent at right angles in two places so that it can be clamped to the operating-table through one of the usual fittings (fig. 1). To the free end is welded a slot to hinge the suspension rod (fig. 2).

With the suspension bar and sand-bag in position the patient can be lifted on and off the operating-table and the towels applied immediately. There is sufficient play in the telescopic suspension rod for the extension of the head to be adjusted so as to maintain an efficient airway, if the anæsthetic is being given to a child via the tongue-piece of the gag. The patient's head rests on the table.



1 2

Fig. 1—The suspension bar.
Fig. 2—The bar carrying telescopic suspension rod and lamp.

Digitized by Google

If the table is tilted or raised, the suspension bar still maintains the same position relative to the patient. The 'Chiron' bulls-eye lamp is fitted to the suspension bar, so it too moves with the table, thus saving unnecessary adjustments.

The advantages over the usual straps and breast-plate for holding the suspension rod are obvious. The breast-plate reduces the respiratory exchange, rendering the patient liable to oxygen lack and carbon-dioxide retention. This alone tends to cause venous congestion, but the effect is supplemented by compression of the veins of the neck by the webbing strap.[1]

The suspension bar illustrated was made by Mr. D. J. Davis, engineer to the Royal Buckinghamshire Hospital. It has been in use in the ear, nose, and throat department for some eighteen months and has proved highly satisfactory.

BRIAN REEVES, F.R.C.S.E.

Reviews of Books

Textbook of Genito-Urinary Surgery

Editor: H. P. WINSBURY-WHITE, F.R.C.S., surgeon, St. Paul's Hospital, London. Edinburgh: E. & S. Livingstone. 1948. Pp. 1046. 90s.

THIS monumental textbook, whose gestation period was prolonged by enemy action, has at last seen the light of day, and proves to be a valuable contribution to British surgical literature. Mr. Winsbury-White and his team of contributors have done well, though inevitably with some overlapping and variation in advice. There are omissions: for example, nothing seems to be said about Hunner's ulcer, a symptom-complex much more commonly met with, or anyhow recognised, in recent years. Partial nephrectomy gets scant attention, and the 25-year-old Canny Ryall lithotrite, the prototype of all effective cystoscopic crushing instruments, is not mentioned. The now widely practised Ombredanne or Denis Browne operations for hypospadias have also been left out, and plastic operations for hydronephrosis and pelvi-ureteric obstructions might well have more detailed consideration. Cystometry is poorly dealt with, and so is urinary incontinence—a disability in the treatment of which British achievement has been second to none. But such criticisms appear carping where there is so much that is good. The chapters on the surgery of the prostate are masterly, written by the chief proponents of the various techniques at present employed; and an excellent summary by the editor follows. Renal tuberculosis, calculous disease of the kidney and ureter, tumours of the testicle, and intestinal transplantation are all covered succinctly and well. The volume is bulky but is plentifully illustrated.

The Thyroid and its Diseases

(2nd ed.) J. H. MEANS, Jackson professor of clinical medicine, Harvard University; chief of the medical services, Massachusetts General Hospital. Philadelphia and London: J. B. Lippincott. 1948. Pp. 559. 72s.

THE first edition of this book, appearing in 1937, gave a comprehensive account of thyroid physiology and thyroid disease, and rapidly established itself as the leading work on the subject. Since then radio-iodine and the antithyroid drugs have invaded the laboratory and the clinic, and their effects on fundamental thought and clinical practice are still difficult to assess. In these and other advances the thyroid clinic of the Massachusetts General Hospital has been notably active. We look to Means, who has been associated with this clinic since its inception in 1913, for an authoritative integration of the old and new knowledge, and are encouraged by his success in achieving another type of integration—that of physiological and clinical modes of thought. He is as much at ease in the language of the laboratory as in that of the clinic: he accepts all knowledge about the thyroid as equally valuable, whether it is derived from a patient or from a laboratory animal, and he believes that all must ultimately benefit the patient. The unity which this attitude produces is most valuable, though in this edition three chapters by other authors somewhat disturb the balance. Fortunately they are by colleagues (R. W. Rawson and Oliver Cope) who share Means's attitude. Yet Rawson's chapters on pathology leave something to be desired, probably because his own contributions to the subject are making such rapid progress that they have become difficult to reconcile with the older anatomical classifications. Cope, in writing on the surgery of the thyroid, has a simpler task, and executes it lucidly. He insists on full pre-operative preparation with an antithyroid drug, rigorous hæmostasis, and a good look at the parathyroids and recurrent nerves.

Those seeking a simple answer to the question: "What is the best treatment for thyrotoxicosis?" will not find it here, though the merits and demerits of subtotal thyroidectomy, antithyroid drugs, and radio-iodine are fully discussed. Means rightly points out that all are unsatisfactory, in that their point of attack is the thyroid. A more satisfying therapy would control whatever makes the thyroid overactive. In the meantime the results of the three methods of attacking the thyroid are so similar that we cannot yet say with confidence which is preferable for any given patient. It may be noted in passing that in this new edition the term "toxic goitre" has given way to the more noncommittal "Graves's disease," and that the chapter on total thyroidectomy for heart disease has disappeared.

Psychoanalysis Today

Editor: SANDOR LORAND, M.D. London: Allen & Unwin. 1948. Pp. 404. 25s.

THIS collection of essays, dedicated to the memory of Sigmund Freud, presents a series of statements by prominent English, American, and European psycho-analysts on the present state of knowledge in their various fields. The essays cover psychosomatic medicine, analytical technique, the theory of the ego, sexual and psychosomatic neuroses, the psycho-analytical theory of psychoses, and approaches to art, religion, and sociology. The level of writing and presentation is high, and the book is particularly interesting to the eclectic in psychology for its clear presentation of modern Freudian theory in practice. The most convincing essays deal with the theory of character development, in which analytical psychology has established its strongest ground. The discussion of schizophrenia is a balanced presentation of the analytical viewpoint, and the relationship of environment, genetics, and organic factors in psychogenesis and treatment; but the essay on affective psychoses is less convincing in its neglect of the mechanisms by which empirical and physical forms of treatment produce their results. Perhaps the most generally interesting contribution is that of Dr. Ernst Simmel on war neuroses, which restates a theory of great sociological interest in the increasingly military structure of modern urban societies. The book is well suited both for the psychologist who needs a concise statement of the psycho-analytic viewpoint, and for the critically minded senior medical student.

Physical Aspects of Colour

The late P. J. BOUMA, Philips Research Laboratories, Eindhoven, Holland. Eindhoven: Technical and Scientific Literature Department. London: Cleaver-Hume. 1948. Pp. 312. 30s.

IN general this is an excellent account of the concepts, units, and methods used in the measurement and specification of colours, written with a combination of simplicity and accuracy which could have emerged only from a mass of detailed and well-digested knowledge. The book is really for the physicist or illuminating engineer who is too intelligent to ignore, but wishes as far as possible to eliminate from his measurements, the complications introduced by the properties of the eye and brain—the very complications that make the subject interesting to the physiologist. Physiologists tempted to theorise about colour-vision must not forget that their purely mathematical concepts and formulæ are attempts to describe, in some universally valid manner, the results of actual experiments with eyes. Of more obvious interest to the biologist are a chapter on colour defectives (though here, for once, the account

1. Mushin, W. W. *Proc. R. Soc. Med.* 1946, 39, 257.

Digitized by Google

is sometimes oversimplified almost to the point of inaccuracy), and a useful history of the development of colour-theory from Newton to the present day. It defines all technical terms, and describes the design and methods of use of most colorimeters; a number of helpful tables and diagrams support the text.

Physics and the Surgeon

H. S. SOUTTAR, D.M., M.CH., F.R.C.S., consulting surgeon, London Hospital. Oxford: Blackwell Scientific Publications. 1948. Pp. 60. 7s. 6d.

THIS is a fascinating little book showing how the principles of physics influence surgical phenomena and are applied in the treatment of disease. Mr. Souttar has presented his material very attractively. We could have wished that in his review of atomic physics he had speculated upon the way in which radiations affect malignant growths; but perhaps this defeated even his fertile imagination.

Ocular Signs in Slit-lamp Microscopy

J. H. DOGGART, M.A., M.D., F.R.C.S., surgeon, Moorfields, Westminster, and Central Eye Hospital, London. London: Henry Kimpton. 1949. Pp. 112. 21s.

APART from the substantial volume by M. L. Berliner, there is no recent text on slit-lamp microscopy. Mr. Doggart's volume is therefore welcome, all the more because it is a concise and adequate presentation, intelligible to the elementary student. Its value is enhanced by the 32 plates with their 85 illustrations in colour. The author has done well in breaking away from the classical approach of the older textbooks which trace the subject historically: the method is now sufficiently established to make its historical development a matter of academic interest. The description of apparatus is reduced to a minimum, and the introductory chapters on the technique of examination and on the normal eye are all that could be desired. Though the account of abnormalities is in the main orthodox, some will question the view that all forms of corneal dystrophy are essentially the same disease. Admittedly the current classification occasionally presents difficulties, but this does not invalidate established findings on different modes of inheritance and different clinical courses of the main types isolated.

The Irish Medical Directory and Hospital Year Book for 1948–9 (Dublin: Parkside Press. Pp. 404. 15s. 6d.) includes new items such as particulars of the Northern Ireland health services, the advisory councils to the Ministry of Health, the Corporation of Dublin health services, the National Insurance Society, and voluntary ambulance and first-aid services.

Traité de thérapeutique clinique (5th ed. Paris: Masson. 1948. Pp. 3696. 3 vols.).—Prof. Paul Savy's large textbook now includes chapters on streptomycin and other antibiotics, and on carcinoma of the prostate, and accounts of therapeutic agents such as heparin and thiouracil. It is still divided into sections according to the organ concerned, each article beginning with a short historical survey. No details of surgical treatment are included, and there are relatively few diagrams and no illustrations. Symptomatic treatment is well covered, the arrangement and writing are clear, and the indexing is adequate, though the paper and printing show signs of present-day shortcomings. It is essentially a working clinical textbook for the general practitioner.

The Invert and his Social Adjustment (3rd ed. London: Baillière, Tindall, and Cox. 1948. Pp. 290. 8s. 6d.).—Mr. R. H. Thouless, PH.D., contributes a preface to the new edition of this book, written by "Anomaly." First appearing in 1927, it is a personal statement of the problems faced by the homosexual male under modern conditions. As an account of these problems it will command widespread sympathy, and the author deals sensibly with the ethical and social adjustments which he has made between his inclination and his acceptance of Roman Catholic teaching. Like previous writers on inversion, he tends to retreat into a defensive solidarity and the assertion of "difference" by which many strongly homosexual individuals protect themselves against the unsympathetic attitudes of society. In the light of what we know of the imperceptible gradation between homosexual and heterosexual patterns of behaviour, emphasis on inverts as a separate community, either of victims or of sinners, is undesirable. The book is most interesting as a study in the invert's assessment of himself, and for some illuminating details of the treatment he receives from the law and from his fellow men. He would, we think, agree with us that the invert and his behaviour, so long as it harms nobody, are without social importance, whatever their connotation in psychosymptomatology; and that any measure which lightens the weight of blackmail, frustration, and public and private persecution would be fully in the interest of society, as well as of the individuals who now have to contend with it.

Principles and Practice of Ophthalmic Surgery (4th ed. London: Henry Kimpton. 1948. Pp. 1044. 75s.).—The new edition of this book by Prof. Edmund B. Spaeth, of Philadelphia, is larger than the last by a hundred pages. Some revision has been necessary, especially in the discussion of implants within Tenon's capsule, a subject in which progress has been considerable in the last five years. The chapters on ptosis, physiology of squint, and extra-ocular muscles have been rewritten, and those on exophthalmos and the plastic surgery of the eyelids revised. Castroviejo writes on corneal transplants and Otto Barkan on goniotomy. Professor Spaeth's text, the most complete work at present published on the subject in English, is representative of all that has been tried and proved in ophthalmic surgery. Many of the illustrations and photographs are also good, but some of the photographs of surgical procedures still leave much to be desired.

Manual of Clinical Laboratory Methods (4th ed. Springfield, Ill.: C. C. Thomas. Oxford: Blackwell Scientific Publications. 1949. Pp. 387. 45s.).—This book, by Prof. Opal E. Hepler, of Chicago, gives in detail the methods of clinical pathology commonly used in laboratories. Since it is not designed to be a comprehensive textbook of clinical pathology, it does not in the main discuss the clinical significance of tests; but where exceptions are, the comments are valuable. In the chapter on urine analysis it might have been useful to mention that false reactions in the guaiac test for blood can be overcome by making an ethereal extract of a boiled and cooled mixture of urine and glacial acetic acid, before adding guaiac and hydrogen peroxide. Full laboratory notes on hæmatological technique are given, and there are chapters on examinations of gastric contents, fæces, sputum, and cerebrospinal and other fluids. The section on bacteriology covers penicillin, streptomycin, and the sulphonamides. Agglutination tests for bacterial and heterophil antibodies are described, and there are well-written chapters on mycology, serology, clinical chemistry, tissue sections, and solutions used in routine tests. This book is well illustrated and includes many tables giving information at a glance. Methods are described in such detail that technicians can follow them with ease.

Subacute Bacterial Endocarditis (2nd ed. New York and London: Oxford University Press. 1949. Pp. 113. 21s.).—Subacute bacterial endocarditis—once almost always fatal—can now usually be cured. The patients live—to die in due course from the effects of previous valvular damage. The emphasis must therefore nowadays be on early diagnosis and adequate treatment, designed to prevent as much valvular damage as possible; for the various peripheral effects, previously so familiar, should now have little opportunity to develop. This monograph by Dr. Emanuel Libman and Dr. Charles K. Friedberg (reprinted from the *Oxford Loose-Leaf Medicine*) is a full account of the subject. The section on treatment is at present up to date, but experience is mounting so rapidly that readers must watch current medical publications for further advances; perhaps more space should have been given to the early and less obvious stages of the disease. Nearly 20 pages are concerned with an account of a small group of cases first described by Libman, in 1913, as the "bacteria-free stage," and characterised by renal failure, severe anæmia, splenomegaly, and brown pigmentation, but no fever, and negative blood-cultures. This seems an extravagant use of space, since such cases were uncommon even before the advent of penicillin. The description of periarteritis nodosa hardly tallies with the modern conception, and the illustrations are rather disappointing, being merely drawings in monochrome.

Digitized by Google

THE LANCET

LONDON: SATURDAY, APRIL 9, 1949

Virus Filaments

UNTIL a few years ago we thought of all viruses as little dots, just below, or perhaps just above, the limits of resolution of the microscope. Ultraviolet microscopy permitted resolution of some of the larger viruses, which were seen to be roughly spherical. For some years the electron microscope seemed only to be showing us larger and larger dots; then it produced its first big surprise—the tailed, tadpole-like appearance of many bacteriophages. Some plant viruses were already known to be rod-like, and this was confirmed by electron microscopy. Improvements in technique have revealed the existence of structural organisation within vaccinia and other of the larger viruses and in the heads of bacteriophages. The size of most virus bodies has proved so uniform that some have doubted whether they could be reproducing by binary fission, for if they multiplied in this way some diplo-forms should surely be seen. Here it must be remembered, however, that almost all who have used electron microscopy have concentrated and purified their preparations, usually by repeated cycles of alternate rapid and slower centrifugation—a technique which naturally sorts out particles of rather uniform size. Is it possible that in consequence something of interest has been missed? This now seems likely.

We know that influenza and some related viruses are adsorbed on to certain red blood-cells. DAWSON and ELFORD [1] lately applied this knowledge by adsorbing such viruses on to the "ghosts" or membranes of laked fowl red cells, and taking electron micrographs, which showed the membranes spotted with adsorbed virus, as if they had a rash. The pictures made it clear that the same method could be used in studying the behaviour of viruses under varying conditions. Moreover, adsorption of virus on to the membranes could be carried out directly from infected chick-allantoic fluids, without resort to the deceptively attractive tricks for sorting out particles of one particular size-range. This new method has quickly yielded something of interest, as the article in this issue by CHU, DAWSON, and ELFORD shows. Strains of influenza-A virus have been coming in to the World Influenza Centre at Hampstead from the recent epidemics in western Europe and elsewhere. Electron micrographs revealed not only the expected round bodies about 0·1 μ across but many long objects—not mere diplo-forms or rods, but worms or serpents up to 10 μ long. Now, in 1946 MOSLEY and WYCKOFF [2] found in influenza-virus preparations a few long forms which they thought were actual viruses; but these forms occurred irregularly and were scanty, so their suggestion could not be tested. Few took it seriously; as CHU and his colleagues say, "the temptation was to dismiss them as artefacts." The pictures we publish today speak for themselves. It is not absolutely certain that the filaments depicted represent a phase in virus development, but weighty arguments are adduced for believing that this is so. To quote only one point, they are visible, by dark-ground illumination, with ordinary microscopes, and can be observed to agglutinate in the presence of homologous antisera.

Strains of influenza A obtained recently from western Europe—and also one from mid-Pacific—are alike serologically and are closely similar to strains obtained in 1947, though widely different from earlier ones. Whereas all the 1947 as well as the 1949 viruses show filamentous forms, strains isolated earlier show fewer or none; but too much significance should not be attached to this since there is some evidence that on propagation in the laboratory round forms gradually come to predominate. The authors are wise not to speculate on the meaning of their observations as regards the life-cycle of the virus. They do, however, draw attention to interesting beaded structures seen within some of the filaments; and they admit that further developments may "revolutionise our conception of the way some viruses multiply."

1. Dawson, I. M., Elford, W. J. *Nature, Lond.* 1949, **163**, 63.
2. Mosley, V. M., Wyckoff, R. W. G. *Ibid*, 1946, **157**, 263.

Sex Hormones in Mammary Cancer

"NOT a cure for cancer, but very profound and gratifying effects" is the claim of Dr. FRANK ADAIR for hormone therapy of breast cancer; and in the course of his address to the Royal Society of Medicine, reported on p. 610, he was able to illustrate "recalcification" of bone metastases and dramatic regression of local skin recurrence and even of metastatic lung masses. Unfortunately these effects are usually evanescent, but even some improvement is an achievement. The sceptic might well recall that PEARCE GOULD,[1] in his Bradshaw lecture of 1910 to the Royal College of Surgeons, described cases *in articulo mortis* where a cancerous growth and its secondaries disappeared spontaneously. Only recently GORDON-TAYLOR [2] described cases "where the axilla was packed with cancerous glands, and no operation could possibly have removed every cancer cell, and yet they remained well for 15–20 years in the absence of postoperative X-ray therapy." But the response to hormones in advanced mammary cancer has been too common for the benefit to be regarded as fortuitous. Not the least impressive feature is the resulting subjective improvement. In 75% of ADAIR's cases pain has been relieved; in most the agony of the bone metastases, particularly of the spine, disappears within a fortnight and narcotics become unnecessary; general malaise and dyspnœa have improved remarkably; and some patients have returned to work. At the same time we should remember DODDS's plea [3] for caution in assessment, because œstrogens may, apart from any specific action, relieve systemic symptoms and provide a sense of well-being. Every surgeon is aware, too, of the receptive mood of the patient with advanced cancer; the patient with hopeless cancer of the stomach will declare himself vastly improved by mere laparotomy.

1. Gould, A. P. *Lancet*, 1910, ii, 1665.
2. Gordon-Taylor, G. *Proc. R. Soc. Med.* 1948, **41**, 118.
3. Dodds, E. C. *Ibid*, 1944, **37**, 736.

Digitized by Google

The hormone therapy of cancer is not a stumble in the dark. In 1935 HADDOW [4] observed that some carcinogenic hydrocarbons retard the growth of malignant tissues; and their slight œstrogenic activity suggested the next step—the trial of synthetic œstrogens. Experimentally, LACASSAGNE,[5] GARDNER,[6] and ALLEN [7] all reported that administration of these was conducive to the development of carcinoma of the breast; and there were several reports of the coincidental development of breast carcinoma during treatment with œstrogens.[8] However, the influence of synthetic œstrogens on prostatic cancer, and isolated reports of encouraging results in breast cancer, indicated the need for their trial in this condition. In 1944 HADDOW et al.[9] described the results of œstrogen therapy in malignant disease as "of considerable fundamental interest . . . and an incentive to further investigation." In the same year contributors to a symposium [10] at the Royal Society of Medicine reported on 168 cases of mammary cancer treated in this way. An important observation appeared. Of 100 cases under the age of sixty, only 1 showed spectacular improvement, while 14 were "improved"; but of 68 cases over the age of sixty, there was dramatic regression in 5 and improvement in 27. The synthetic œstrogens seemed to influence mainly the skin lesion, and bone metastases were relatively unaffected. The dosage used, as DODDS commented, was small—at most 15 mg. daily—and took no account of insensitivity to the drug. The evidence of inactivation of œstrogens in the body which emerges from a review by ZWARENSTEIN [11] shows clearly the need for trial of higher dosage. (In prostatic cancer some workers are already using 1000 mg. a day, with due precautions.) However, œstrogen therapy is probably not the answer for the woman under sixty; and HERRMANN and his colleagues [12] assert that it may even accelerate extension of the tumour.

In 1938 LOESER [13] suggested the use of androgens. Later he proposed [13] pellet implantation of the hormone in the wound at the time of operation—a practice now followed by ADAIR—and he further recommended yearly implants of 3000 mg. or more, as a prophylactic measure. The war and the scarcity of supplies interrupted work in this country; but in America PRUDENTE [14] reported a 90·4% three-year postoperative survival-rate without recurrence in patients who received prophylactic treatment of this sort. FARROW,[15] on the basis of a small dosage, had reported adversely; but other accounts, by ADAIR and HERRMANN,[16] were encouraging. A dose of 100 mg. three times a week became the general rule, and according to ADAIR 200 mg. daily is being used in some clinics. LOESER held that the need for massive dosage "may be gauged from the fact that a preponderance of at least 50 : 1 must be secured . . . to counteract the female hormones . . . where the œstrogen level is normal." Such heavy doses have to be given with care, especially to the cardiac patient; for they cause sodium, potassium, and nitrogen retention, usually with consequent development of œdema. Moreover, some of the masculinising effects cannot be ignored: patients develop facial hirsuties, pimples on the body, enlarged clitoris, and increased libido.[17]

The mechanism by which hormones produce their effect is not yet clear. With œstrogen therapy KOLLER [9] found in serial biopsies that "cell degeneration may be due to a breakdown of the mitotic mechanism." With testosterone the most prominent biochemical change is the increase of blood-calcium, up to 17 mg. per 100 ml.; and ADAIR [16] speculates on a "snowing under," and a "locking in by the process of calcium precipitates"; certainly biopsies indicate that the cancer cells do not disappear. In the osteoporotic skeleton of the aged, calcium mobilisation may be dangerous, and TAYLOR and his associates [17] advise the application of a brace in the early months of treatment. Later, according to ADAIR, the blood calcium seems to settle. LOWENHAUPT and STEINBACH,[18] who have attempted to use the histological grade of malignancy as a guide to hormone therapy, report that the lower grades appear to be controlled more effectively, and they advocate concomitant X-ray therapy for the tumour of high malignancy. Their findings differ somewhat from those of MCWHIRTER and PATERSON,[10] who found the cellular growths more responsive to hormones.

Any new therapy may be followed by a wave of indiscriminate enthusiasm. It is well to bear in mind that CUTLER and SCHLEMENSON,[19] who treated 20 cases with adequate dosage, believe that sterilisation produces similar results, whether induced by operation or X rays. To 85% of early cases without involvement of the axillary glands, radical mastectomy offers the brighter prospect of a five-year cure.[20]

Implantation of Insulin

To be able to take insulin by mouth is the dream of every diabetic. MURLIN and his colleagues [21] tried a mixture of insulin and hexyl resorcinol in twenty diabetic patients, but with little success; and capsules of insulin and quinine, tested by CUTTING and his associates [22] either failed completely or produced a very irregular effect. The position with regard to administration of insulin by mouth was summed up by JOSLIN in these words: "all preparations on the market claiming to control diabetes when taken orally are, by and large, quack medicines." [23] Practically every other alternative to injection has been tried, including inunction or absorption

4. Haddow, A. *Nature, Lond.* 1935, **136**, 868.
5. Lacassagne, A. *C. R. Soc. Biol. Paris*, 1938, **129**, 641.
6. Gardner, W. *Arch. Path.* 1939, **27**, 138.
7. Allen, E. *Endocrinology*, 1942, **30**, 942.
8. Allcaben, G. R., Owen, S. E. *J. Amer. med. Ass.* 1939, **112**, 1933. Atkins, H. J. B. *Lancet*, 1940, ii, 411. Auchincloss, H., Haagensen, C. D. *J. Amer. med. Ass.* 1940, **114**, 1517.
9. Haddow, A., Watkinson, J. M., Paterson, E., Koller, P. C. *Brit. med. J.* 1944, ii, 393.
10. *Proc. R. Soc. Med.* 1944, **37**, 731.
11. Zwarenstein, H. *Clin. Proc., Cape Town*, 1946, **5**, 83.
12. Herrmann, J. B., Adair, F. E., Woodard, H. Q. *Arch. Surg.* 1947, **54**, 1.
13. Loeser, A. A. *Brit. med. J.* 1938, ii, 320; *Lancet*, 1941, ii, 638; *Obstet. Gynec. Surv.* 1948, **3**, 363.
14. Prudente, A. *Surg. Gynec. Obstet.* 1948, **80**, 575.
15. Farrow, J. H. *Surgery*, 1944, **16**, 141.
16. Adair, F. E., Herrmann, J. B. *Ann. Surg.* 1946, **123**, 1023; *J. clin. Endocrinol.* 1946, **8**, 769. Adair, F. E. *Surg. Gynec. Obstet.* 1947, **84**, 719.
17. Taylor, S. G., Slaughter, D. P., Smejkal, W., Fowler, E. F., Preston, F. W. *Cancer*, 1948, **1**, 604.
18. Lowenhaupt, E., Steinbach, H. L. *Surg. Gynec. Obstet.* 1949, **88**, 291.
19. Cutler, M., Schlemenson, M. *J. Amer. med. Ass.* 1948, **138**, 187.
20. *Proc. R. Soc. Med.* 1948, **41**, 118.
21. Murlin, J. R., Gibbs, C. B. F., Romansky, M. J., Steinhausen, T. B., Truax, F. L. *J. clin. Invest.* 1940, **19**, 709.
22. Hanzlik, P. J., Cutting, W. C. *Endocrinology*, 1941, **28**, 368. Cutting, W. C., Robson, G. B. *Ibid*, p. 375.
23. Joslin, E. P., Root, H. F., White, P., Marble, A., Bailey, C. C. Treatment of Diabetes Mellitus. London, 1947.

Digitized by Google

through the conjunctivæ, rectum, and vagina; but all have failed through the irregularity of the results and the large amounts of insulin required. Even intravenous injection is undesirable, because the action, although rapid, is of unpredictable duration. For all practical purposes, therefore, the only reliable mode of administration is by subcutaneous injection.

With the aim of reducing the frequency of injections, methods have been evolved for delaying absorption of insulin from the subcutaneous tissues. One of the earliest reports was that of POULTON and his team [24] at Guy's Hospital, who succeeded in retarding absorption somewhat by giving the insulin in a 20% solution of gum-arabic. Some years later LEYTON,[25] after experimenting with suspensions of insulin in various oils (including arachis oil, which he discarded because of the pain it caused on injection), finally adopted a suspension in castor oil. In laboratory animals, the action of insulin injected subcutaneously has been prolonged by the addition of magnesium, zinc, iron, or tannic acid; but BAVIN and BROOM [26] showed that with more than a trace of the metal the normal insulin response was completely inhibited. A practical advance came with the introduction first of protamine-zinc insulin, and subsequently of globin insulin with zinc; and the popularity of these two forms indicates their efficacy and the very real need they have met. The article in this issue by VARGAS, who describes his results with the implantation of insulin pellets, marks the latest development in the attempt to ease the diabetic's lot.

Following upon his success with compressed tablets of steroid hormones implanted subcutaneously, PARKES [27] turned his attention to the administration of insulin in this way. With YOUNG,[28] he found that in rabbits crystalline or low-zinc insulin acted for about as long when implanted as a tablet as when injected subcutaneously. Later he established that in rats the action could be prolonged by implanting pellets containing 10–25% of crystalline insulin and cholesterol; but in male rats these pellets proved lethal.[29] VARGAS and his colleagues found in rabbits made diabetic with alloxan that the subcutaneous implantation of pellets containing protamine-zinc insulin and cholesterol controlled the diabetes satisfactorily. On the basis of these findings, VARGAS has now tested this treatment in man. Although initial results are promising, the method he describes can plainly not come into general use at once. In most patients the diabetic state fluctuates so much that treatment cannot be standardised; often the dosage of insulin has to be changed at quite short intervals. Moreover, though the implant continuously gives out insulin, it cannot strictly be regarded as an artificial pancreas, for there is no evidence that the rate of insulin release will be influenced, as in the pancreas, by such factors as the level of the blood-sugar and the secretions of the pituitary or thyroid. Further work may show how these disadvantages can be minimised.

24. Burgess, N., Campbell, J. M. H., Osman, A. A., Payne, W. W., Poulton, E. P. *Lancet*, 1923, ii, 777.
25. Leyton, O. *Ibid*, 1929, i, 756.
26. Bavin, E. M., Broom, W. A. *Quart. J. Pharm.* 1937, **10**, 327.
27. Deanesly, R., Parkes, A. S. *Proc. roy. Soc.* B. 1937, **124**, 279.
28. Parkes, A. S., Young, F. G. *J. Endocrinol.* 1939, **1**, 108.
29. Parkes, A. S. *Ibid*, 1942, **3**, 220.

Measures of Morbidity

IN the last few years several countries have been thinking of extending their system of vital statistics to include the statistics of illness. Rates of mortality, particularly at their present low level, are felt to be insufficient, and sometimes too insensitive, for the public-health and social-medicine worker. Interpretation of sickness figures may, however, present real difficulties. The distinction between the living and the dead is perfectly clear, but a much less decisive line divides the healthy from the ailing. Moreover, whereas death occurs once and at a specified point in time, illness may recur; and it occupies a period whose beginning and end are often ill defined. How is sickness to be measured? Perhaps by incapacity for work; but the duration of this incapacity will depend to some extent on the nature of the employment, and on social and economic factors. The present need is not so much for a definitive system of sickness recording or analysis as for experiment. For example, the value of hospital statistics in this context, and of general practitioner's certificates, are being investigated; the application of survey methods to small but representative samples of the population are being tested; and the information from sickness absence records in factories and workshops might also be studied.

A particularly opportune contribution comes this week from the General Register Office. In the second of its new series of occasional publications, entitled Studies on Medical and Population Subjects, Dr. PERCY STOCKS [1] analyses sickness in the population of England and Wales in 1944–47. His material comes from three sources: (1) notifications of infectious diseases, (2) the monthly survey of sickness carried out through the Social Survey, and (3) certifications of certain scheduled diseases made to entitle patients to special food allowances (which will, we may hope, be only a temporary source of statistical information).

Writing on the notifiable infectious diseases, STOCKS points out that the criterion for notification is that the person is "suffering from" the disease.

> The isolation from the patient's body of the causative organism "does not constitute the presence of the disease, nor do thoracic shadows on a skiagram, nor skin or serum reactions to biological substances." In other words, bacteriological, biological, and radiological tests are aids to diagnosis, but "the temptation to use them as measures of disease incidence without regard to whether the subject was 'suffering from' anything must be resisted if epidemiological statistics are to have any meaning." Subclinical attacks—e.g., of poliomyelitis—may be difficult to deal with; but clearly if the attack is believed to be one of the specified disease, then, however mild, it must be notified.

These particular statistics have been more valuable since 1944, when quarterly returns by sex and age were first collected. How much clearer would have been the reasons for some of the steeply declining death-rates—from measles, scarlet fever, and diphtheria, for instance—if we had had an age-distribution of those attacked in, say, 1900. We might then have known how far the reduced mortality is due to improved treatment and care, and how far to postponement of the attack, in the modern small family, till an age when death is less likely. STOCKS concludes

1. Sickness in the Population of England and Wales in 1944–47. H.M. Stationery Office. Pp. 51. 1s.

Digitized by Google

that today notification is fairly complete for poliomyelitis, cerebrospinal fever, diphtheria, and scarlet fever, but in defect by some 10% for respiratory tuberculosis, by 20% for the enteric fevers, and by 30% for measles; he estimates that of pneumonia cases only a third to a quarter, and of whooping-cough cases even less, are notified. It is thus very possible that some of the recorded attack-rates will rise appreciably in the next few years if, under the health service, the doctor's help is more freely invoked.

A table of the notified cases of acute poliomyelitis and polioencephalitis brings out the magnitude of the 1947 epidemic. In 1944–46 the average rate of notifications was 1·7 per 100,000 persons of all ages, whereas in 1947 it was 18·3—an elevenfold increase. This order of increase is apparent at each age; so the outbreak does not appear to have been at all selective by age. In regard to cerebrospinal fever, STOCKS estimates that at present rates of inception, 1 in 240 children will be notified before reaching the age of fifteen. The tuberculosis position will be dealt with more fully in a later report, but it is noted here that whereas during the inter-war years 5 out of 10 persons notified died subsequently of the disease, the proportion has now fallen to 4 out of 10. It seems more likely that milder cases are now being brought into the notification figures than that the fatality-rate has fallen generally.

The notification statistics of the infectious diseases are, if not exactly ancient, at least of respectable antiquity; and they are freely used as broad measures of epidemic events. The Social Survey of sickness, on the other hand, is a recent experiment which must be—as our American friends would say—"validated." Informants are asked about illness in the two previous months; and the statistics reveal, as would be expected, difficulties in recalling the date when an illness began. It appears that this failure of memory tends to bring into the period illnesses which in fact began outside it—an error that will to some unknown extent compensate for illnesses that have been forgotten altogether. Another difficulty is in deciding whether people's own accounts of their maladies are reliable; and here, says STOCKS, "the patient often has to decide whether or not he is ill at all." A check of the incidence-rates produced by these self-reported illnesses against some of those yielded by notification of infectious diseases or through food permits suggested that the statements are pretty reliable; but the check is, of course, not wholly convincing, since the other two sources supply information only about certain diseases, usually serious and therefore easily remembered, particularly if, while a food allowance is being drawn, an "official" interviewer calls to ask about illness. Whatever its shortcomings, the survey does collect much information that would otherwise not be gathered into the statistical net; for of those reporting an illness, only 1 in 7 has stayed away from work (or, in the case of a housewife, been confined to the house), and only 1 in 4 has consulted a doctor; only 1 in 9 of men of working age who say they have been indisposed have stayed away from work for as long as four days—the minimum period that would usually bring the illness into the National Insurance statistics. It may be asked whether this vast mass of "illness" is so slight as hardly to justify the heavy task of recording it. The answer will depend on whether the results can throw light on changes in the state of the public health, on whether the exponents of social medicine can base health measures on these results, and also on whether epidemiology—a term which by modern usage we can extend to all disease—will be advanced.

The final section, on the statistics of priority allowances of foods given for certain diseases, reveals (at the end of 1947) approximately 100,000 diabetics in England and Wales, or about 2·3 per 1000 of the population; 4467 cases of thyrotoxicosis (at the end of 1945) with a sex ratio of about 1 male to 3·5 females; and 118,000 cases of respiratory tuberculosis receiving priority milk, or 2·8 per 1000 persons. The figures for gastric and duodenal ulcer are curious. The total number in England and Wales in December, 1945, was roughly 342,000, and a year later it was of the same order—339,000. By March, 1947, it had risen to 382,000, and by December of that year to 437,000. The explanation is perhaps a more earnest attempt by dyspeptics to secure the priority allowances rather than an increased prevalence.

In a brief introduction the REGISTRAR-GENERAL promises further studies, to be devoted to tuberculosis, accidents, and migration. The object of the series, he says, is "to provide in convenient form a more extensive treatment of important subjects than is practicable within the limits of the Annual Review." One might add that there is also gain in not burying these readable studies within covers that are rarely opened except by statisticians. With these two opening numbers Dr. STOCKS has certainly given the series a rare start.

Annotations

BRITISH MEDICAL GUILD

DURING the last three revealing years the British Medical Association has learned much about its own strengths and weaknesses, when it is faced with the task of negotiating with the Government and with other public bodies. In particular it has found that it is precluded by its own constitution from any activity that might be held by a court of law to be one that could properly be performed only by a trade union. It was for this reason that the Independence Fund and its trustees were established; it would have been deputed to undertake organised opposition against the National Health Service Act had that been the will of an effective majority of the profession. The crisis which then passed may not be the last that will have to be faced, and so the representative body of the association debated last week what changes are needed to provide machinery for representing grievances in the future, and for organising pressure if necessary. Three possibilities were canvassed. The first was that of leaving the association in its present form except for revoking the clauses in its constitution which limit its syndicalist activities. This would in effect turn the present association into a limited company and would have disadvantages both in nomenclature and in liability to taxation. The second suggestion was that the association might be turned into a trade union (or failing this into a friendly society). It was found that neither change could be made easily. In law it was doubtful if a group of doctors could successfully claim to be a group of workmen, or of employers, and they might therefore not qualify for the protection given to such specified groups by the Trades Disputes Act. In any case, conversion to a trade union or a friendly society could not be undertaken without first winding up the existing association, and distributing all its assets among

Digitized by Google

its present members. Therefore, after long discussion, a third course (and the one favoured all along by the council) was accepted. This was to form a parallel organisation—in appearance not unlike that of the Independence Fund and its trustees—which will be known as the British Medical Guild.

The guild is to have no membership. It will in effect be but a board of trustees. The trustees will consist of any or all of the members for the time being of the central council of the B.M.A., who have individually given their assent to serve. The guild will, when so required, endeavour to rouse support and organise action in favour of the association's policy as then current. To finance the guild's activities, and to provide resources from which it could indemnify doctors who suffer loss or hardship through participation in collective action, there will have to be substantial funds. These funds it is hoped will be raised within reasonable time by voluntary subscription from the profession.

Time alone will show how powerfully and successfully such an organisation can act. Meanwhile the association is fortified by learned legal opinion that the proposed guild could carry out its intended functions of organising and financing collective action by the profession, and of providing financial compensation to practitioners suffering financial hardship through participation in such collective action, without in any way endangering the life or position of the association itself.

AN EPIDEMIC OF THYROTOXICOSIS

BETWEEN 1942 and 1945 a remarkable increase in the incidence of thyrotoxicosis was recorded in Denmark. The rise, and subsequent fall, in the number of cases was abrupt enough to justify the use of the term "epidemic," though without implying that any infectious agent was concerned. The facts have been recorded with admirable thoroughness by Iversen in a monograph [1] published in 1948, and now summarised elsewhere.[2]

Iversen's detailed figures relate to all cases in Copenhagen entering hospital for the first time with the diagnosis of thyrotoxicosis; and he found that the incidence in the whole country ran parallel to that in the capital. His figures show that there was a slow increase in incidence from 1938 to 1941. In 1942 there was a rapid rise, with a further slight increase until the peak was reached in 1944. After that there was a sharp fall, till in 1947 the incidence was the same as in 1940. Iversen feels confident that his records include virtually all cases of thyrotoxicosis in Copenhagen, and he is able to state actual figures for the incidence of the disease. Thus, in 1938 there were 0·19 cases per 1000 inhabitants; in 1944, 0·83; in 1947, 0·21. The chances of an inhabitant of Copenhagen developing thyrotoxicosis were about four times as great at the height of the epidemic as before or since.

The increase was, he believes, real, and not simply the result of better diagnosis. It cannot have been due simply to the psychological effects of the German occupation, for it started during 1941, when the behaviour of the invaders was comparatively mild, and it showed only a slight further rise in 1944, when the Germans "got tough." Moreover, during the same period the incidence and severity of thyrotoxicosis in Belgium tended, if anything, to decrease.[3] In Holland also there seems to have been a fall,[4] while in Norway a small increase in incidence in the early stages of the German occupation was followed by a fall.[5]

Two other factors may have played some part—weather and diet. Iversen points out that the winters of 1940, 1941, and 1942 were unusually severe, and there is experimental evidence that exposure to cold stimulates the thyroid. It is not perhaps very likely that the hard winter of 1942 would still be causing fresh cases of thyrotoxicosis in 1944, but this possibility cannot be excluded, since Iversen's cases are grouped by the date, not of onset, but of entry into hospital. During the German occupation the diet of the Danish people varied comparatively little, and was never grossly deficient as in Belgium and Holland. Iversen's suggestion in this connexion is ingenious, if rather far-fetched. Before the war large quantities of soya-bean oil were imported as cattle-feed; these imports ceased in 1941. Soya bean is well known to contain an antithyroid factor, and this factor might be contained in the cattle-feed and subsequently in the cow's milk (though this has never been proved); cutting off the supply of this factor might unleash a series of fresh cases.

If we review the events in Belgium, Holland, Norway, and Denmark as a whole, the least unacceptable theory seems to be that the invasion of these countries by the Germans did increase the tendency of the inhabitants to develop thyrotoxicosis, but that this tendency was masked in the case of Belgium and Holland by the highly abnormal diet. The masking effect of the diet might be due to lack of calories or of protein, or to excess of vegetables containing antithyroid factors. This theory gets its chief support from the experience of Norway. There the diet remained adequate during the first year or so of the German occupation but became deficient later; and an initial increase in thyrotoxicosis was followed by a decrease at about the time when the diet deteriorated. It is tempting to suppose that the increase was caused by the psychological effects of invasion, and the decrease by the poor diet; but there is no certain proof.

1. Iversen, K. Temporary Rise in the Frequency of Thyrotoxicosis in Denmark, 1941–45. Copenhagen, 1948.
2. Iversen, K. *Amer. J. med. Sci.* 1949, **217**, 121.
3. Bastenie, P. A. *Lancet*, 1947, i, 789.
4. Schweitzer, P. M. J. *Acta. med. scand.* 1944, **119**, 306.
5. Grelland, R. *Ibid*, 1946, **125**, 108.

TRANSMISSION OF LIGHT THROUGH SKIN

DURING the last years of the German occupation and "in the course of evening hours," Dr. Hansen [1] investigated the transmission of light through the skin. After preliminary experiments he chose to work with a Philips super high-pressure mercury arc-lamp (capable of emitting a constant supply of ultraviolet rays giving "a quasi-continuous spectrum") and a photo-electric cell for estimating the intensity of the transmitted light. He compared transmission through skin excised from the mouse immediately after death or during anæsthesia, skin stored in an ice-chest, skin from pedicle grafts, skin obtained at necropsy, and skin removed at operation or after blistering. He found that all except the stored skin gave almost identical and constant curves. Transmission through stored skin was greater, but the curves were similar. He concludes that within the wave-lengths 500 mμ and 300 mμ the course of the transmission curve is the same for live mouse skin, for skin excised shortly after death, and for frozen sections of both types of skin, decreasing uniformly with the wave-length from 500 to 300 mμ, with a minimum at 415 mμ, attributed mainly to hæmoglobin absorption. The various layers of skin are not characteristic in their absorption of radiation, and there is nothing in the results to indicate that there is any wave-length region to which a specific biological effect on skin tissue can be ascribed.

The only uncertainty left by these careful experiments is whether the current from the photo-electric cell is proportional to the intensity of the light falling on it. Hansen says he investigated this point at four wave-lengths (313–450 mμ) and found that it was proportional, but he admits that this is contrary to accepted opinion and offers the explanation that the light intensities he

1. On the Transmission through Skin of Visible and Ultraviolet Radiation. By K. G. HANSEN. *Acta radiol., Stockh.* 1948, suppl. 77. Pp. 106. Sw. Kr. 8.

Digitized by Google

used were small. Since the validity of the curves depends on this point, his findings require confirmation; but they appear to be a valuable addition to our knowledge of the subject.

STREPTOMYCIN IN TUBERCULOUS MENINGITIS

A REPORT issued by the Scottish Therapeutic Trials Committee summarises the results of streptomycin treatment in 81 cases of tuberculous meningitis which have been followed for at least four months. The drug was given by both intramuscular and intrathecal injection; the intrathecal injection was usually repeated daily for two to three weeks, either continuously or during alternate weeks, after which a single weekly injection was given for several months. Of the 81 cases, 38% are said to be "progressing favourably." This percentage rises to 58% in the 4–17 age-group, compared with 24% below and 21% above these limits. Favourable progress is reported in 33% of 52 patients followed for at least seven months. The prognosis was considerably worse with miliary tuberculosis of the lungs or with choroidal tubules. The writers recognise that the percentage of successes may fall as the period of observation is extended. Unfortunately the series, though it provides interesting data, was too small to permit assessment of different techniques of treatment; and we may hope that analysis of the much larger series treated in English hospitals will incidate which schemes of treatment give the best results.

CONTINUED CARE AT CAMBRIDGE

IT will be many years before Addenbrooke's Hospital is rebuilt; and meanwhile the governors of the Cambridge United Hospitals are faced with long waiting-lists, a shortage of nurses, and a shortage of hospital beds. To increase the turnover of the beds they have, they are considering the formation of a home care and nursing service which should enable patients to return more rapidly to their own homes. A committee presided over by Sir Lionel Whitby have suggested that an experimental service for about thirty patients should be started, restricted in the first place to the borough of Cambridge. The hospital consultant staff, they propose, should decide what cases are suitable for transfer from hospital to home; but they foresee that minor surgical cases, cases of malignant disease, rheumatic diseases, and other chronic ailments requiring little skilled nursing would be suitable. As the service grows, psychiatric cases may be included and physiotherapy and occupational therapy may be developed. The aim is to provide nursing and domestic help; medical care will be the responsibility of the patient's family doctor, backed by consultant opinion when required, for the patients will sometimes need further expert advice. They must be sure of readmission to hospital when necessary.

To make a scheme like this work, many people will have to combine good-humouredly—the local health authority, the hospital consultants, the general practitioners, the district nurses, the home-help service, the ambulance service, and the hospital almoners. It happens that in Cambridge the district nurses are not working to the limit of their capacity, and they foresee no difficulty in meeting moderate demands from the new service; indeed, they are cheered by the promise of unusually interesting cases. A training school for district nurses is already projected and should help to replenish personnel. The home-help service is already efficient, and could be made to grow to meet the new demands on it. The general practitioners are thought to be willing (though, as things stand at present, they cannot be offered special remuneration); consultants will give domiciliary consultations under the Act; and the ambulance service exists. The almoners are ready enough to help as soon as they can be relieved of some of their work by the appointment of a records officer in their department. Most of the staff are thus already at hand and receiving appropriate rewards. The committee think that the scheme could be run by adding a lay director, man or woman, who would be responsible for coördinating the service and receive a salary of £500 a year (not very much, surely, for the director of a service which is intended to grow?) assisted by a shorthand-typist receiving £300 a year. They estimate printing, stationery, and telephone costs at £100 a year, and so foresee a total annual outlay of less than £1000. The governors believe they could meet this cost, with the consent of the Ministry of Health, out of ordinary hospital expenditure; but there is no reason, the committee have been informed, why the Ministry should not itself support the scheme, and they have hopes that outside bodies might assist the experiment if asked to do so. Already, under the National Health Service, each local health authority is required to provide district-nursing and home-help services; though obviously a long time is going to elapse before they all live up to that requirement.

It will be remembered that for some years Dr. E. M. Bluestone has run a "department of continued care" from the Montefiore Hospital, New York.[1] There the scheme has proved not only a valuable but an economical social service, the cost working out at $3 a day for the patient in his home, compared with $10 a day for an inpatient. The Cambridge proposals also have something in common with the scheme for the care of old people in their homes, introduced at St. Helier Hospital, Carshalton, by Dr. E. B. Brooke.[2] The committee at Cambridge believe that the new venture incidentally "offers an opportunity for unobtrusive research in sociology, which would therefore be of interest to the university department of human ecology." However that may be, it certainly offers an opportunity for more care and comfort to more sick people.

THE KING'S HEALTH

THE following bulletin was issued from Buckingham Palace on March 30:

> The King continues to make good progress after his recent operation. In order to secure the continuation of the natural process of formation of collateral circulation which has been encouraged by the operation, we have advised His Majesty that a prolonged period of convalescence will be necessary.
>
> MAURICE CASSIDY — J. R. LEARMONTH
> THOMAS DUNHILL — J. PATERSON ROSS
> HORACE EVANS — JOHN WEIR.

It is not expected that a further bulletin will be issued for some time.

The King has appointed Dr. JOHN GILLIES, reader in anæsthetics in the University of Edinburgh, to be a commander in the Royal Victorian Order.

A Home Office committee, with Sir Ernest Gowers as chairman, has just reported on statutory regulation of the hours of employment of young persons, and statutory provisions relating to health, welfare, and safety at places of employment not covered by the Factories, Mines, or Quarries Acts. It recommends that statutory restrictions should be extended to all occupations other than agriculture, forestry, fishing and shipping, private domestic service, and outworking. Only about 7½% of juveniles in employment would remain outside the codes, compared with about 35% at present. The report, obtainable from H.M. Stationery Office (Cmd. 7664, Pp. 115, 2*s*.) makes recommendations for reform in the various occupations considered. The committee included Dr. A. J. Shinnie.

1. Cherkasky, M. *Modern Hospital*, May, 1947; see *Lancet*, 1947, ii, 213.
2. See *Lancet*, March 12, p. 462.

Digitized by Google

Special Articles

INTRAVENOUS PROCAINE
A REVIEW

WILLIAM W. MUSHIN, M.A. Oxfd, M.B. Lond., F.F.A.R.C.S., D.A.
DIRECTOR

L. RENDELL-BAKER, M.B. Lond., D.A.
SENIOR ASSISTANT

DEPARTMENT OF ANÆSTHETICS, WELSH NATIONAL SCHOOL OF MEDICINE, AND UNITED CARDIFF HOSPITALS

THE intravenous injection of procaine was for long regarded as an accident to be avoided. Numerous reports appeared through the years alleging that such an occurrence, usually inadvertent during local anæsthesia, resulted in collapse and sometimes death. Now, intravenous procaine is being advocated for the alleviation of symptoms in a host of unrelated conditions ranging from allergy to angina and pruritis to parturition.

The injection of procaine into a vein to produce local anæsthesia of a limb was described by Bier (1909); a tourniquet was advised to prevent the entry of the drug into the general circulation and to prolong the anæsthesia. It was not until some 25 years later that the subject was revived and procaine was deliberately injected intravascularly, first for endarteritis obliterans by Leriche and Fontaine (1935) and then two years later for tinnitus aurium by Lewy (1937).

A brief mention of intravenous procaine appeared in a textbook on anæsthesia by Lundy (1942), who noted its effectiveness in relieving the pruritis of jaundice. Within a year Gordon (1943) reported on intravenous procaine analgesia for the dressing of burns in war casualties, and commented on the absence of the respiratory depression often seen when large doses of morphine are used for this purpose. The interest of English-speaking anæsthetists and surgeons was aroused, for it became evident that comparatively large amounts of procaine injected intravenously could be tolerated by man provided the injection was made slowly.

During and immediately after the war, French workers were developing the clinical use of this therapy independently, but along slightly different lines. The French work on this subject has lately been described by Ameuille (1948). The most promising use of this therapy, to the French workers, appeared to be for the relief of dyspnœa due to a variety of pulmonary and cardiac causes.*

MODE OF ACTION

Procaine, which is diethylaminoethyl-*p*-aminobenzoate, belongs to the alkamine ester group of compounds (Dawes 1946a and b). These compounds all have a similar basic structure, by variation of which their main action resembles that of atropine, curare, an anti-histaminic, or a local anæsthetic (Ing et al. 1945). In addition to the main action they may show several of the other effects to a lesser degree. Some, like 'Benadryl,' 'Anthisan,' and 'Antistin,' are potent anti-histaminics, while possessing atropine-like and local anæsthetic properties at the same time. Others, like procaine, have, besides their local anæsthetic action, atropine-like, curare-like, and probably anti-histaminic effects as well.

Procaine and the other local anæsthetics among these esters are now known to have a quinidine-like action on the auricle of the heart (Dawes 1946a and b), which probably explains the efficacy of procaine in stopping fibrillation and other cardiac arhythmias. The anti-histaminic action probably accounts for its striking effect in urticaria and other allergic manifestations, and many of procaine's properties may be the result of its antagonistic action to acetylcholine, for conduction in the heart muscle resembles that in sensory nerves, and Burn (1948) suggests that acetylcholine plays an important part in this conduction. Vasodilation, too, may be the result of antagonisation of acetylcholine by procaine at the synapses in the sympathetic ganglia.

Clinically, intravenous procaine has a powerful effect in relieving pain of both sympathetic and somatic origin. An oversimplified explanation of this and other effects is in terms of that pharmacological classic—Dixon's law. This says that the concentration of a local anæsthetic required to block the sympathetic fibres in a mixed nerve is lower than that for the sensory fibres, and that again is lower than the concentration for the motor fibres. Procaine, when injected intravenously, concentrates seven to eight times more in inflamed tissues than in normal, as a result of the increased capillary permeability in the diseased tissues responsible for the pain (Graubard and Ritter 1947). The still very low concentration of procaine in these tissues during the course of this therapy would be expected to have its first effect on the nerve terminals of smallest diameter—the sympathetic fibres and those conducting pain impulses.

CLINICAL USES

Relief of Pain.—The types of pain for which intravenous procaine has been advocated are many and varied, and the following are but a selection: post-operative pain, both in the operation wound (McLachlin 1945), and that associated with chest complications; the pain of dressing burns (Gordon 1943), angina pectoris (Graubard et al. 1948b); thrombophlebitis (Barbour and Tovell 1948); intermittent claudication of vascular disease (Leriche and Fontaine 1935); and arthritis (Graubard et al, 1948a). It has even been used as an analgesic in labour, with, in the hands of enthusiasts, good results for mother and child (Allen 1945, Allen et al. 1946, Johnson and Gilbert 1946).

Our own experience of intravenous procaine as an analgesic is limited to its use during the dressing of burns, and for the relief of pain during the first twenty-four hours after abdominal operations. A high degree of relief is obtained, with a notable absence of respiratory depression. The method, however, needs constant skilled medical attention.

Vascular Diseases.—Since Leriche and Fontaine (1935) first described the use of procaine in vascular diseases it has been advocated for thrombophlebitis, coronary disease, pulmonary embolism, Buerger's disease, and poor peripheral circulation generally (Graubard et al. 1948b). Some writers suggest that intravenous procaine is of at least as much value as sympathetic block.

Cardiac Surgery.—The ability of procaine to reduce the irritability of cardiac muscle has been known for many years (Kochmann and Daeles 1908, Hermann and Jourdan 1931, Mautz 1936, Beck and Mautz 1937, Shen and Simon 1938). At one time it was applied to the surface of the heart, because its effect on arhythmias was thought to be due to its local anæsthetic action on the cardiac sympathetic nerve-endings. Procaine is in fact nearly as active as quinidine on the heart. It is of interest that amethocaine, another local anæsthetic, is some ten times as active as quinidine (Dawes 1946a and b). Burstein et al. (1940) have clearly demonstrated that arhythmias provoked during 'Cyclopropane' anæsthesia by the injection of adrenaline can be prevented or cut short by the intravenous injection of procaine, and that even after ventricular fibrillation has developed normal rhythm can be restored by the intracardiac injection of procaine. These experimental findings have been substantiated by many anæsthetists. (Burstein 1946, Bittrich and Powers 1948, Barbour and

* Benda and Benda (1946) claim that *p*-aminobenzoic acid, a closely allied compound, is as effective as procaine and less toxic.

Digitized by Google

Tovell 1948). Many make a practice of giving an intravenous procaine drip throughout thoracic operations when the heart is to be handled and arhythmias are anticipated.

Allergic States.—Several writers (State and Wangensteen 1946, Appelbaum et al. 1946, Dressler and Dwork 1947) describe a dramatic retrogression of symptoms and signs after intravenous procaine in serum sickness and penicillin-sensitivity reactions, though the mode of action in these conditions was by no means clear until recently, when the close relationship between procaine and the anti-histamine drugs was established (see Burn 1948). Procaine has also been advocated for asthma (Durieu et al. 1946). We have experience of one case of status asthmaticus of some 24 hours' duration in which adrenaline and atropine were of no avail and the patient was exhausted and appeared in extremis, but the slow intravenous injection of 10 ml. of 1% procaine dramatically ended the attack.

FATE IN THE BODY, TOXICITY, AND DOSAGE

Procaine is broken down in the liver into *p*-aminobenzoic acid and diethylamino-ethanol (Fosdick and Hansen 1931). This breakdown also occurs, in part, in the blood-stream by the action of an enzyme (Goldberg et al. 1943). So far no significant biochemical upset in the body as a result of procaine therapy has been observed. Liver function is unimpaired (Jacoby et al. 1948).

An optimal intravenous dose of procaine gives the patient a feeling of warmth and relaxation. If this optimal dose is exceeded or administered too quickly signs of overdose appear—"pins and needles" in the hands and feet, dizziness, twitching, convulsions, and ultimately loss of consciousness. Vitamin-C deficiency increases the liability to these side-effects (Richards 1947); in fact, some advocate the addition of ascorbic acid to the procaine solution before use (Graubard et al. 1948b). Another precaution to reduce the possibility of convulsions is the previous administration of a barbiturate.

The elimination of a therapeutic dose of procaine from the blood-stream occurs within 20 minutes (Graubard et al. 1947). Therefore, if a prolonged effect is desired, the injection of procaine must be repeated frequently, or the procaine must be administered as a continuous infusion of a dilute solution. Except in emergencies, the continuous drip is most satisfactory and a dilution of 0·1%—1 g. of procaine in 1000 ml. of normal saline—will be found convenient.

For an optimal effect from a single dose, 25 mg. per stone (4 mg. per kg.) of body-weight, given as an infusion of a 0·1% solution in twenty minutes, is recommended (Graubard et al. 1947). Where a longer and less intense effect is desired the same dosage given at a slower rate suffices.

In emergencies, such as ventricular fibrillation, status asthmaticus, severe angina, or pulmonary embolism, up to 10 ml. of 1% procaine solution (100 mg.) may be given as a single intravenous injection. A careful watch should be maintained for the onset of convulsions and a syringe containing thiopentone kept handy as an antidote.

SUMMARY

Procaine injected intravenously possesses well-marked analgesic, quinidine-like, anti-histamine, and anti-acetylcholine properties. Its versatility as a therapeutic agent is indicated by the following uses to which it has been put:

1. As a generalised analgesic for pains due to a variety of causes.
2. As an emergency treatment for, or prophylactic against, cardiac arhythmias. It is a valuable addition to the armamentarium of the anæsthetist during thoracic operations.
3. As treatment for various allergic and allied conditions—e.g., serum sickness, penicillin-sensitivity reactions, asthma, and urticaria.
4. As a treatment for vascular disease, where it may take the place of a sympathetic block.

Intravenous procaine is easily administered, but vigilant supervision is necessary if overdose is to be avoided.

REFERENCES

Ameuille, M. P. (1948) Medical Research in France during the War 1939–45. Paris; p. 263.
Allen, F. M. (1945) *Amer. J. Surg.* **70**, 283.
— Crossman, L. W., Lyons, L. V. (1946) *Anesth. & Analges.* **25**, 1.
Appelbaum, E., Abraham, A., Sinton, W. (1946) *J. Amer. med. Ass.* **131**, 1274.
Barbour, C. M., Tovell, R. M. (1948) *Anesthesiology*, **9**, 514.
Beck, C. S., Mautz, F. R. (1937) *Ann. Surg.* **106**, 525.
Benda, R., Benda, P. (1946) *Sem. Hôp. Paris*, **22**, 1577.
Bier, A. (1909) *Münch. med. Wschr.* **1**, 589.
Bittrich, N. M., Powers, W. F. (1948) *Anesth. & Analges.* **27**, 181.
Burn, H. J. (1948) The Background of Therapeutics. London; p. 89.
Burstein, C. L. (1946) *Anesthesiology*, **7**, 113.
— Marangoni, B. A., Degraff, A. C., Rovenstine, E. A. (1940) *Ibid*, **1**, 167.
Dawes, G. S. (1946a) *Brit. med. J.* i, 43.
— (1946b) *Brit. J. Pharmacol.* **1**, 90.
Dressler, S., Dwork, R. E. (1947) *J. Amer. med. Ass.* **133**, 849.
Durieu, H., de Clerq, F., Duprez, A. (1946) *Acta clin. belg.* **1**, 150.
Fosdick, L. S., Hansen, H. L. (1931) *Dent. Cosmos*, **73**, 1082.
Goldberg, A., Koster, H., Warshaw, R. (1943) *Arch. Surg.* **46**, 49.
Gordon, R. A. (1943) *Canad. med. Ass. J.* **49**, 478.
Graubard, D. J., Kovacs, J., Ritter, H. H. (1948a) *Ann. intern. Med.* **28**, 1106.
— Ritter, H. H. (1947) *Amer. J. Surg.* **74**, 765.
— Robertazzi, R. W., Peterson, M. C. (1947) *Anesthesiology*, **8**, 236.
— — — (1948b) *Anesth. & Analges.* **27**, 222.
Hermann, H., Jourdan, F. (1931) *C.R. Soc. Biol. Paris*, **106**, 1153.
Ing, H. R., Dawes, G. S., Wajda, I. (1945) *J. Pharmacol.* **85**, 85.
Jacoby, J. J., Coon, J. M., Woolf, M. P., Salerno, P. R., Livingstone, H. M. (1948) *Anesthesiology*, **9**, 481.
Johnson, K., Gilbert, C. R. A. (1946) *Anesth. & Analges.* **25**, 133.
Kochmann, M., Daeles, F. (1908) *Arch. int. Pharmacodyn.* **18**, 41.
Leriche, R., Fontaine, R. (1935) *J. Chir., Brux.* **34**, 537.
Lewy, R. B. (1937) *Arch. Otolaryngol.* **25**, 178.
Lundy, J. S. (1942) Clinical Anesthesia. Philadelphia.
Mautz, F. R. (1936) *J. thorac. Surg.* **5**, 612.
McLachlin, J. A. (1945) *Canad. med. Ass. J.* **52**, 383.
Richards, R. K. (1947) *Anesth. & Analges*, **26**, 22.
Shen, T. C. R., Simon, M. A. (1938) *Arch. int. Pharmacodyn.* **59**, 68.
State, D., Wangensteen, O. H. (1946) *J. Amer. med. Ass.* **130**, 990.

THE PROBLEM OF HOME ACCIDENTS

(FROM THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, PUBLIC HEALTH DEPARTMENT)

HOME accidents—what a mixed bag of domestic misfortunes the phrase suggests! Yet when they are picked up and examined, there are features enough in common to make a study of their general or group causes worth while. With our knowledge of the means of preventing these accidents still woefully insufficient, even a limited exploratory survey research deserves attention.

At the request of a "panel" of the Scientific Advisory Committee of the Ministry of Works, a group of a dozen students at the London School of Hygiene was formed into a seminar to plan and execute a small home-accidents survey. The results of the investigation were interesting on their own account, but statistical information was inevitably slight. A number of special difficulties in method of inquiry and assessment of findings were brought to light. The following report deals with these.

J. M. M.

* * *

Every year 15,000 people in England and Wales die as the result of an accident: road accidents account for 6000 and industrial accidents for 2000. The greater proportion of the remainder can be classified as accidents in the home. For each person killed many more receive less serious and non-fatal injuries.

To obtain a little information on this latter group of non-fatal home accidents a survey was carried out by post-graduate students of this school. The survey covered a period of four months. During that time six hospitals (all except one being situated in Central London) notified

Digitized by Google

505 outpatients, of whom 150 were visited in their homes. For each case visited a four-page schedule was completed, covering all aspects of the case—medical details, the family, overcrowding, structure of the house, psychological features including accident-proneness, and precautions taken, in order that the fullest information should be available for deciding the cause of each accident, and the means by which it could have been prevented.

The immediate purpose of the survey was to study methods of inquiry. The results were demonstrated by means of an exhibition, and a dramatic act based on our experience.[1] More leisurely analysis and consideration of the data have prompted this contribution to the problem of home accidents. We have naturally compared our results with those obtained by other investigators and by other methods, and we want to stress certain features of the data which are not always borne clearly in mind.

BIAS IN OUR SOURCES OF INFORMATION

Any one source of information, taken alone, is bound to be biased and unrepresentative. The Registrar-General analyses and presents all the deaths from accidents, but he can tell us nothing about the patients who recover. The injuries which are rarely fatal are overlooked, while those which obey the "all or nothing" law, such as electrocution, suffocation, and poisoning, receive undue attention. In addition, changes in incidence-rate and fatality-rate cannot be observed.

Even for deaths, sufficient information to decide whether it is a home accident is not always forthcoming; the cause is not always apparent, and the means which would have prevented the accident are rarely discernible. Attempts may be made to gain this additional information from coroners' inquests, but here again the possibility of bias (in the statistical sense) enters. Certain types of accident are more likely to come to inquest, because they are surrounded by some mystery. In addition, the limelight focused on these tragedies by the very fact of there being an official inquiry may be prejudicial to eliciting the finer psychological points which may be so important.

A similar type of bias is involved in the collection and statistical analysis of press cuttings, as is done for Government departments interested in these accidents. The cases most likely to be reported are those which will excite the emotions of the newspaper readers—sex interest (women in burning nightgowns), politics (explosives found in coal), the heartstrings of mother love (suffocated babies). Further distortion and misplacement of emphasis can readily occur during the editing and cutting. Above all, in any fatal accident, we are up against the difficulty that dead men tell no tales.

NON-FATAL ACCIDENTS

Our sources of information for non-fatal accidents are just as precarious. Some investigations have been made into special types of injuries, such as burns and scalds, in hospital inpatients, and in a limited number the circumstances of the home have also been investigated. These cannot be considered representative of all types of accidents, since all social classes do not use the hospitals to the same extent, and all kinds of accidents do not need, in the same degree, admission to hospital.

Another approach has been to investigate accidents met with in the houses visited by health visitors. They naturally found a high proportion of accidents in young children and housewives, and one can understand the tendency shown to exonerate the patient, and to lay the blame on the inanimate environment. The police have also made a survey: they were not so chary of moral censure. Being on the spot immediately after the accident and being by training on the look-out for drunkenness, it is natural that they should find a relatively large proportion of accidents due to drunkenness.

The survey based on outpatients notified by the hospitals in Central London clearly revealed the numerous sources of bias in our method of approach. It was known from other sources[2] that only a fraction of the incapacitated seek advice at hospitals, and it was speedily realised that it is not necessarily the severity of the lesion that leads to hospital attendance. A cut which bleeds calls for spectacular treatment: a humdrum crushed finger or twisted ankle is disregarded. An anxious mother will hurry to hospital with her child: her own injury is neglected until brought to light by a routine attendance at an infant-welfare clinic.

Comparison of the hospitals revealed differences in their notifications. On the whole females predominated except at the extremes of age, yet one hospital notified more males than females. Some hospitals served an area lying within only a few miles of the hospital: the patients of others were spread well beyond the bounds of Greater London. Curious offshoots were found, determined either by the attraction of easy transport routes, or connexions with local practitioners, or by faith in central hospitals.

Notification does not mean the same thing to all hospitals. One will notify everything that might conceivably be a home accident, so that a large proportion need to be rejected after investigation; another hospital, whose almoners carefully sift the records, does the preliminary screening so thoroughly that nearly all unsuitable material is discarded. A hospital with a centralised records department could easily report on any patient in or attending the hospital; while another with separate registers for outpatients, for casualty, and for fracture clinic, and its inpatient records distributed on every floor of the hospital would find considerable difficulties.

The attempt to visit the homes of the patients caused further selection. Some addresses were never found, and inexperience and lack of local knowledge may have contributed in some degree to these failures; other addresses were located, but the alleged patient was not known there, and it seems that a small proportion of patients gave misleading addresses. Patients living far afield were not visited, and others seemed to be always at work or not at home to callers. For those finally run to earth the scope of the investigation varied considerably. We found, as have others, that women are most successful at these front-door interviews, better able to break down any "snooper resistance" and to obtain entry to the house, and confidences about any family skeletons. In assessing the cause of the accident there is ample scope for individual judgment: two assessors may weight the human and the inanimate causes very differently in the same case, or the same assessor may find the accent misplaced when reviewing a case-history at a later date.

FURTHER RESEARCH

The approach to home accidents differs from that towards accidents in industry or in the Services. In the latter, the main object is to weed out the unsuitable or accident-prone person. We cannot take this attitude towards the housewife: we have to accept people living in the home. There may be an analogy between the new entrant to industry, and the young infant facing the unknown dangers of the hearth and stairs, but the results of inquiry into industrial accidents are not immediately applicable to home accidents.

An accident is the result of human action, and accident research is a subject for psychological study. It has been noted that after an accident the patient tends to adopt one of two extreme attitudes, either blaming himself

1. See *Lancet*, 1948, I, 758.

2. Slater, P. Survey of Sickness, Social Survey. 1946.

Digitized by Google

mercilessly for his own "carelessness," or exculpating himself completely, and laying all the blame on the material environment. It was interesting to observe the incredulity of some patients that we should think an accident should have any cause—"Why, it was a pure accident, doctor!"

The possibility of explaining accidents on the basis of Freud's theory of everyday mistakes and slips has been suggested. Here is an example within our recent experience: an elderly woman, who was known to be jealous of her husband's popularity with the ladies, was presiding at the tea-table. The conversation turned to her husband, who was away being photographed with the matron and nurses of the hospital with which he was connected. The flippant conversation was interrupted by the wife knocking over the hot-water jug, and being scalded on the leg and foot, accidentally. Yes, a genuine accident, but what an effective way of changing the subject, and attracting attention and sympathy. Unless one is present during the occurrence of the accident, and on the look-out for such psychological causes, it is difficult to disinter them later, and particularly difficult at a street-door interview with a slightly suspicious housewife. There is a tendency to reject such motivated explanations[3]; to determine how important they are needs intensive or introspective research, and is a field where the general practitioner's personal knowledge of the patient would be an asset.

In the past attention has been focused on major accidents, and minor injuries have tended to be ignored. In our first list (of 15 notifications) there were 5 attendances as hospital outpatients for "fish-bone in throat." These we brushed superciliously aside, but regretted having done so later when we found that this type of injury appeared to come in epidemic waves—as if some particular consignment of fish, or some vagary of the weather or the meat situation had a bearing on its incidence. Foreign bodies in the eye, again, hardly seemed worthy of attention, but when we reflect how commonly it happens to every one of us, in a minor form, and how frequently treatment is sought outside of hospitals, it assumes an added importance.

Accidents are fortunately fairly rare in the experience of any one individual—sufficiently uncommon to make experimental procedures and the testing of preventive methods a matter of difficulty. This is an argument in favour of the study of minor injuries, which are relatively more frequent. It has been suggested, in the case of traffic accidents, to use some manifestation which occurs more often than accidents—say to observe the number of people who step carelessly into the road. In pilots once a correlation between accidents and a certain type of reaction has been established, the reaction may be used as an indicator in experimental studies.[3] The need is to find some attribute closely connected with domestic accidents—possibly lack of attention, use of makeshifts, slovenly movements, minor injuries, and abrasions—so that without waiting for an accident to happen, one may judge of the likelihood of an accident happening.

Further knowledge is required about the "exposure to risk" in various accidents. For example, a third of all falls in the home were found to occur on the stairs; and since the time spent on the stairs is very much less than a third of our waking hours, one may safely conclude that stairs present an increased hazard. It was also found that only one fall in the series occurred on carpeted stairs, but it is impossible to draw any conclusions about the safety or otherwise of carpeted stairs unless we know the proportion in the general population of houses. Background knowledge such as this—the proportion of houses with steep stairs, with winders, with structural defects—is essential before the statistics from accidents can be fully interpreted. The guidance of expert social investigators, with adequate secretarial and statistical facilities is desirable to make the best use of the medical personnel.

The general practitioner, with his facilities for easy access to houses, both for accidents and other diseases, is in a singularly fortunate position for accumulating data of this kind.

The survey of sickness carried out by the Social Survey has shown that sick persons seek treatment not only from their own doctors and from hospitals, but also from chemists and factory nurses; or they may not go to any outside agency. Any investigation limited to one angle of approach can give only a partial and biased picture, but by combining together different approaches—especially through the hospitals and through general practitioners—a truer picture of accident incidence and composition will be obtained. It will not necessarily be complete, but it will be less incomplete than any existing survey.

3. Pilot Error, A.P. 3139A. Air Ministry, 1948.

NEW ZEALAND HOSPITAL SALARIES

FROM A CORRESPONDENT

UNDER a new award,[1] the salaries of whole-time hospital medical officers are to be increased throughout New Zealand.

The medical superintendent-in-chief at Auckland is to receive £2000 rising to £2250, while at Wellington the figures are to be £1900 and £2150 respectively. The salaries of the superintendents of smaller hospitals are to range from a minimum of £1250 to a maximum of £1500; and at Christchurch and Dunedin the minimum is to be £1650 and the maximum £1900. Three scales are provided for specialists, with minima ranging from £1050 to £1750 and maxima from £1350 to £2000. Whole-time medical officers not otherwise provided for are covered in six scales ranging up to a maximum of £1550.

Even with these increases the salaries of whole-time hospital doctors will compare unfavourably with the earnings of general practitioners. In a recent lawsuit the head of a medical combine in Dunedin sued a colleague for possession of a consulting-room; and the defendant stated in his evidence that his gross takings for eighteen months amounted to £8600, or nearly £5750 a year. Small wonder that with such figures as these before them, many parents see in medicine an unusually lucrative future for their children, and that in consequence the medical school is filled to overflowing. Steps have had to be taken to limit the number of entrants by making the first medical examination competitive. Those already qualified are no doubt rejoicing that this method did not exist in their time.

Overcrowding is no new phenomenon. Prof. L. S. P. Davidson, now on a visit to the Dominion, lately told the press that with 120 medical graduates a year the doctor's economic position would deteriorate, so there would be no need for further provision for medical education by opening a new medical school in Auckland; and the present dearth of research-workers would be righted because the promising graduates would not be diverted into the golden path of general practice.

The relation of cause and effect is doubtless as difficult to estimate in the realm of economics as in medicine, but there is every reason to suppose that the publicity given to medical earnings can have done no-one any good. The doctor who sees his neighbour, the mechanic, setting out with his family for the beach on a Saturday morning will say that if a 40-hour week is good enough for one it is good enough for another, and will refuse to answer a weekend call. The mechanic, who cannot get a doctor to visit him, and who may be dissatisfied with the care he receives when he does, will

1. See *Lancet*, March 26, p. 537.

Digitized by Google

wonder why the doctor should be receiving ten times his own income; and this may be one of the factors at the root of the present industrial unrest now coming to the surface in a go-slow movement by the Auckland carpenters, with resultant dismissals and boycotting of firms which refuse to give employment to the displaced workers. The New Zealand Federation of Labour is at present applying for a general wages' increase which will add £25 million to the country's annual wages' bill. The following extract from the proceedings of the Court is at least suggestive:

Mr. BAXTER (Secretary of the Federation of Labour): "Much of the discontent among workers today is due to an instinctive resentment that other sections of the community are getting away with considerably more than is justified under stabilisation."

Mr. JUSTICE TYNDALL: "I think much of the discontent may be due to propaganda and oratorical eloquence."

Mr. BAXTER: "That is only a minor factor. . . . The workers are suffering from a feeling of frustration and a feeling that they are not getting the same in comparison with other people."

Mr. JUSTICE TYNDALL: "They wouldn't know that if someone had not told them."

Disabilities

27. PAROXYSMAL AURICULAR FIBRILLATION

FOR about five years my heart has been fibrillating intermittently, and though the reality of the fibrillation has been confirmed by electrocardiography, no doctor has yet found an organic cause. I am 52, and my heart seems exceptionally efficient. I have neither breathlessness nor any other symptom of heart disease; there are no positive signs, apart from the fibrillation, and my blood-pressure is 120/76 mm. Hg.

The difference between fibrillation and no fibrillation is sharp, like the difference between having the electric light on and off; there is no half-way house, and the moment when fibrillation starts can be fixed to a second or two. It is less likely to start if my attention is held by something congenial. It often begins in moments of emotional conflict, and the attack never stops when I am thinking about it—and it is a most uneasy feeling, difficult to avoid thinking about. In between the attacks the pulse-rate slows down steadily by about 4–6 beats per minute per day until, after 3–6 days, the rate is below 60 and I feel that there is something a bit missing in the middle of the chest. Then a new fibrillation may start. Anything which increases the pulse-rate—for example, climbing a cliff—helps to reduce this uneasy feeling in the chest and to defer the next attack; but there comes a point at which the reverse holds—lying still prevents fibrillation, and then any sudden movement such as straining, sneezing, getting off a bicycle, or even fetching a bucket of coal may start it. Other circumstances that have set it going include crawling under a hen-house to try to catch hens which have gone to roost there owing to the pophole having been accidently shut too soon; a feeling of indecision between two courses of action; somebody speaking to me when I am listening to the wireless or trying to talk to someone else; an ambivalent attitude by someone I'm speaking to (frank hatred or rudeness do not bother me); and any feeling of excitement which does not lead to action. My very first attack, five years ago, was connected with uneasiness about my son's bed-time. Both my wife and I want him to go to bed at the right time; but whereas she has always thought that this should be left largely to him, I have always feared that, left to his own devices, he might get too little sleep.

The fibrillation, though unpleasant, seems to relieve something in the chest. During an attack the sensation, aggravated by exercise, is of something adrift inside, but I am not at all breathless or fatigued; I continue to sleep and eat well, and my life is not disturbed. Occasionally there is slight, superficial pain in the muscle in the upper part of the chest near the shoulder. Formerly the attacks used to occupy about 35–40% of the total time; but two years ago it was discovered that I had diabetes (which, with the help of insulin, is fully controlled) and now it takes up about 48% of the time. Despite this increase since the diabetes was detected, there seems to be no correlation between the attacks and the blood-sugar level. For about a year I took digitalis, but the effect of this was inconclusive. On two occasions long attacks, lasting 15 and 8 days, have been stopped within three hours by 0·4 g. quinidine; 0·2 g. had no apparent effect. Phenobarbitone, which I have been taking lately, seems to help in preventing attacks. Rest does not seem to stop an attack; but I have noticed that it is stopped by such varied events as sudden fright when driving a car; making an unpopular speech to a rather hostile audience; solving an interesting mathematical problem; finding an interesting book in an uninteresting bookshelf; reading for the first time Bohr's original 1913 paper on the hydrogen spectrum in the *Philosophical Magazine*, after being excited by its ideas for twenty-seven years; having a rather difficult discussion when acting as tutor of a rural Workers' Education Association class; carrying two suitcases across a station and successfully getting them into the left-luggage office despite every difficulty; and finding a fallacy in a philosophical argument.

In a well-known experiment two doors are presented to a dog. One door has a circle painted on it, the other an ellipse. If the dog goes through the circle, he gets a bone; if through the ellipse, an electric shock. He learns to choose the circle. Ellipses of diminishing eccentricity are now chosen until the dog cannot distinguish between the two doors and has a nervous breakdown. By similar method a flock of neurotic sheep has been raised; and an octopus has been made neurotic. It seems that in my case fibrillation is associated with a similar kind of neurotic state, though this does not account for the purely mechanical methods of starting an attack that I have described, nor for the steady slowing of the non-fibrillating pulse. I feel that this curious cardiac disturbance—and possibly the diabetes too—is only a symptom: but whether what it is trying to tell me is physical, mental, or spiritual, I don't know. It may be spiritual. I have for the past eighteen years been convinced of the need to be genuinely religious; I see clearly through the non-religious view, and yet I find it incredibly difficult to be religious myself. Perhaps this situation constitutes a minor spiritual conflict. There is no doubt that some of the greater spiritual struggles—for example, that of St. Catherine, of Genoa—did produce startling cardiac symptoms.

I have consulted doctors in plenty. In what they say they present a completely united front; but by the expression on his face each gives the impression that—anyhow in dealing with an odd state like mine—he doesn't believe what his colleagues have told him. In the end all have been surprised—and convinced. Though myself sure of the functional origin of the symptoms, I have been rather dismayed at the readiness of the three psychiatrists that I have consulted to accept this explanation without examining me. If, as I believe, the root cause of my trouble is a "worry," I wish someone would tell me exactly what that worry is; then I could, I think, do something to cure myself. Is there perhaps room for further research into the correlation of emotional conditions with various types of disease? I do at least know that fibrillation is not amusing: I want no more of it.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

IT'S a great relief to me that ours is not really a teaching department. In many ways we have an ideal chief—always accessible, unruffled, and ready to absorb the troubles that might otherwise upset our work. But once in a while the picture changes. Normally in close touch with the work of the department, he begins to retire from sight. There are long unexplained absences, from which he emerges with a pregnant, harassed look. For the next week he is with us, at least in body. But he is not himself. In writing reports we use with impunity such black-balled phrases as " prior to," " has a tendency to," and " in a marked manner." Occasionally a request from him for a fact here or a reference there tells us that though isolated he is not totally detached from reality. But there comes a day when we begin to doubt even that. He will pick up at random a pen and some bits of paper, and disappear. Five minutes later he is back, big with thought, speaking hoarsely, and looking toxic; he deposits paper and pen on the bench ready to repeat the cycle. This goes on till someone suggests that he might gather strength from lunch. In this phase he will come into the lab as if seeing the place for the first time; and he passes his oldest associates with a glassy stare. Last week at the height of a very bad attack a distinguished colleague, normally greeted with the civility the chief extends to all, was brushed away with a vague: " Hello, you here again? " I drew the visitor aside to explain delicately the chief's interesting condition. He was a learned physician, and knew the remedy. " Never let him know that he has to speak until the actual morning of the lecture." Well we can but try—at least it will shorten the period of gestation.

* * *

I haven't been doing consultant work very long—only a few months—so I am still receiving hard knocks on my vanity at regular intervals; but this is the worst to date.

I was asked to see an old lady in the country who had a large rodent ulcer. After examining her with the dignity that becomes a specialist, I solemnly pronounced that the condition was not serious provided suitable treatment was given at once. " Well, Doctor," she said, " I'm glad to hear that. To tell the truth we were in two minds whether to call you in or to ask the charmer down the road to treat it." Ten years' study, culminating in a battle-royal with the London censors, and still only a lucky short head in front of a charmer. It makes you think.

* * *

From the Waikato, one of New Zealand's most flourishing dairy districts, comes news of what may be one of the triumphs of penicillin. Starters in the cheese factory refused to start, and the experts suggest that the trouble may be due to penicillin used in treating mastitis in some of the cows of the district. Cheese in the Dominion is of three kinds—" tasty " (an edible variety of Cheddar), " mild " (mousetrap), and " process" (******); so sabotage in the cheese industry, though it may mean less for the Old Country, will be hailed with joy by all conscientious tyrophagists.

Cheese. What memories the word evokes! For me it recalls the first, and alas the last, meeting of the Chichester cheese-eaters. It all began in the shop of a connoisseur who sold the most noble Cheddars from an establishment, since blitzed, in Southsea. Over a prolonged degustation of these gems he promised me a share of his next consignment of Talleginos, " the best of all the soft cheeses." Armed with this hope I bade my messengers ride forth to spy the country for specimens worthy to appear on the table with these treasures. From a shop in Salisbury High Street came news of a splendid Caerphilly; a store in Oxford Street was reported to keep a fine collection of the home country kinds; and a shop in Kingston-on-Thames to be the repository of some magnificent soft cheeses from the Continent.

And what a feast it was! In front of each guest was a plate of biscuits and a lordly dish of butter. Then, when their appetites had been whetted by a bowl of minestrone with parmesan, a cloth was drawn from the sideboard, and there lay the cheeses—Stilton, Caerphilly, Lancashire, and Cheshire, Wensleydale and Gouda, Gorgonzola, Leicestershire, Brie, Tallegino, Gruyère and Parmesan, Cheddar and Dutch, Roquefort and Danish blue, Camembert, St. Ivel, Bel Paese, Port Salut; and great flagons of cider to wash them down. But that was in the England of long, long ago. Here we send the fat from the milk to England and give the protein to the pigs. Come, New Zealanders, throw the " process " out of the window and raise your glasses to Florey, Fleming, and Chain.

* * *

Until recently, whenever I had a " hang-over " after a night of jollification with kindred spirits, I gave myself scant sympathy, and grimly awaited the healing hand of time. Since the report of the Departmental Committee on Industrial Diseases was published in November, 1948, however, I have got a new slant on my periodic indispositions. In this report disease is defined as " any departure from health capable of identification by its signs and symptoms." Clearly, then, the " morning after " is more than I thought, and I ought to be thankful for my survival. In the new light I can see myself—a sick man—staunchly pursuing my professional career through many weary hours when I should have been having all the care appropriate to my temporary but readily identified departure from health. In future I must see my panel doctor about a certificate.

* * *

In France I used to collect specimens of argot. There were vivid terms like *tord-boyaux* (literally, twist-guts, which may be rendered as griper) for any strong—and bad—eau-de-vie. Then there was the conjugation of the present indicative of the verb " to sleep " beginning only with the usual word:

je dors	*nous ronflons*
tu roupilles	*vous en écrasez*
il pionce	*ils piquent un somme*

Now I am making a similar collection in the U.S.A., and, without competing with the imaginative masterpieces lately seen in the *New Statesman*, I can already offer a like version of the phrase " to be drunk ":

I am as drunk as 40 dollars	We are boiled
You are as high as a kite	You are petrified
He is fried	They are as high as a Georgia pine

One takes it for granted that one has to learn the French language, with argot as a supplement, but it is not enough just to learn American slang as a supplement to one's English. One has to learn the American spoken language itself, which is—I believe—extraordinarily energetic, pungent, and vivid, full of striking idioms, metaphors, and similes. It is only by hearing it daily that one can appreciate it and overcome the common English prejudice against it.

It is easy enough to buy a dictionary of slang, but one can't try to learn up hundreds of words, which may be of local or of special use, or which may have died an early death. However, I have found both French and American friends keen to instruct me in the lore and my American collection grows daily. It probably amuses them to hear their native slang uttered incongruously with a strong foreign accent. It fazes (embarrasses) me that, apart from a few special types, such as Service slang, our English equivalent seems now to be such small potatoes or mere peanuts.

* * *

After weeks of tribulation and argument the young wife had persuaded her middle-aged husband, suffering from melancholia, to go for treatment into the local mental hospital. After saying a touching farewell to the patient she gave the house-physician a full history of the misery of their lives. Next day he received a letter from her saying: " Dear Doctor, I forgot to tell you that my husband tried several times to cut his wrist with a razor blade. I enclose a few razor blades for him. I am sorry I could not get more, but they are scarce in the shops here. . . ."

Digitized by Google

Letters to the Editor

THE ROYAL COLLEGES

SIR,—Mr. R. T. Payne's letter of March 5 calls for further comment on the position which the colleges occupy today.

They are in good company in taking an active interest in the subject of remuneration of medical men: the Vice-Chancellor of Cambridge University has addressed the Senate on it, and *Nature* has mentioned it in a leader; so the time when academic science can safely stand remote from practical affairs must surely have passed. Such is the unwilling but sincere opinion of a number of fellows of colleges which is considerable though quiet. They chose to act upon it when their views differed from those of the British Medical Association (though, if to differ from B.M.A. policy is a crime, Mr. Payne is not entirely free of guilt). They have since done their best to remedy the division in the profession, and, as one who urged such a course in your columns, I feel that what they have done should be recognised. Their highest officers have formed a committee with the elected representatives of B.M.A. consultants and specialists, nobody barred. Any physician, surgeon, obstetrician, or gynæcologist elected by his fellows can meet the president of his college face to face and tell him exactly what he thinks. If Mr. Payne were on that committee his vote would be as good as Lord Webb-Johnson's. This Joint Committee of consultants and specialists has met the Ministry: all official decisions are given in the presence of both parties. As far as the suspicion of undue influence can be removed the statesmanship of both sides has removed it, and I believe that the act of faith which this remarkable gesture constituted is having its reward in mutual understanding, respect, and support.

Compared with this, the advantages of subscribing to the Fellowship for Freedom in Medicine grow unfortunately less with every decision they take and statement they issue.

Hove. W. A. BOURNE.

TOXICITY OF TRIDIONE

SIR,—Information about severe toxic reactions from any new drug has to be viewed in the context of the total number of patients treated and the therapeutic results. Recent reports of the toxicity of 'Tridione' should therefore be considered together with Lennox's [1] estimate of 10,000 cases treated in the U.S.A. with this substance, to which probably some hundreds must be added from this country. Reported fatalities from both countries now number 8, with a further 6 cases of severe though reversible poisoning. In 2 of these the responsibility of tridione for the changes was in doubt. On this view, toxicity cannot be regarded as very high; and the benefits are certainly great.

However, such statistical considerations will never reduce the individual tragedy of a preventable death: and Dr. Forster and his colleagues (March 26) rightly insist on frequent and full blood-counts in tridione treatment. I would suggest that careful clinical supervision is almost more important. The earliest manifestations of a toxic blood dyscrasia, from tridione as from other substances, are probably slight general symptoms—sore throat, malaise, listlessness, and loss of the normal sense of well-being. If patients and their family doctors are aware of this, apparently trivial complaints may be a valuable warning of the need to stop the drug and check on the blood. With patients attending hospital at intervals, such early changes must be watched for in the home.

During the past year and a half we have treated over 50 patients in this clinic with tridione. A significant granulopenia, reversed by stopping the drug, occurred in 2 cases. In one, the parents remarked on slight general changes in the child's health some time before the blood-count was done. An acneiform rash is a common occurrence, and is usually unaccompanied by further toxicity. The rash may, however, be absent in cases which show blood changes, and it is therefore of little value as a warning of more severe reactions. If the drug produces no benefit, it should of course be stopped; and a prompt review should also be made if its previous therapeutic effect ceases. Toxic effects on skin and blood, if appreciated early, are usually rapidly reversible. Moreover, they often do not recur at all when the drug is restarted after a rest period. These disturbances should be seen in perspective as calling for vigilant but continued use of a valuable remedy.

Department of Neurology, Radcliffe Infirmary, Oxford. C. W. M. WHITTY.

1. Lennox, W. G. *J. Amer. med. Ass.* 1945, 129, 1069; *Ibid*, 1947, 134, 138.

OXYGEN THERAPY IN SHOCK

SIR,—I was glad to read, in your issue of Jan. 15, Dr. Ohlsson's letter recommending oxygen therapy in the prevention and treatment of traumatic shock. As a transfusion officer in the field, I came across a number of cases where, in my opinion, lives might have been saved if at that time oxygen therapy had been available in ambulance cars.

According to Dr. Ohlsson, the therapeutic effect of oxygen inhalation depends on improved oxygenation of the arterial blood. He says that, mainly by the physical absorption of oxygen by the plasma, oxygen carriage is increased by 2 ml. per 100 ml. of blood. In my opinion this increase may well be the main beneficial factor in cases where no hæmoconcentration has occurred (that is, in the prevention of traumatic shock), but the increase will be on a smaller scale in fully developed shock, when hæmoconcentration has taken place, because here the amount of plasma and thus its oxygen-carrying capacity is greatly diminished. Benefit from oxygen therapy may then be due to a different cause.

It is known that in traumatic shock the tissues are able to take up more oxygen from the blood than normally; the oxygen content of the venous blood is decreased because the coefficient of oxygen utilisation is increased. Cordier [1] found that in animals dying in shock, the affinity of the blood for oxygen is reduced; thus the removal of oxygen in the tissues is facilitated and the coefficient of oxygen utilisation increases. But at the same time oxygenation in the lungs is naturally rendered more difficult; and Underhill [2] and Cordier showed that blood leaving the lungs may not be fully saturated. This disability is overcome by the inhalation of oxygen. The blood then leaves the lungs fully saturated, and as a result of the greater coefficient of oxygen utilisation the tissues may receive, say, 12 ml. instead of 6 ml. of oxygen per 100 ml. of blood. Thus the improvement in oxygen delivery to the tissues is about three times as great as it could have been by increased oxygen absorption alone. The effect will in fact be still greater because the decreased affinity of the blood for oxygen is associated with hæmoconcentration and increased oxygen capacity of the blood.

The characteristic changes in the blood during shock—namely, diminished oxygen saturation in the lungs and the greater utilisation of oxygen in the tissue—are fully explained by the diminished affinity of the blood for oxygen. This really means that the affinity of hæmoglobin for oxygen is diminished. Such a condition could be brought about by various factors, of which changes in the concentration of hæmoglobin *inside* the red blood-corpuscles would be the most potent. I have found such changes with phosgene poisoning in dogs.[3] The results differed according to whether the animals died in shock or recovered—i.e., according to the severity of the condition. In animals dying of phosgene poisoning, the average hæmoglobin concentration inside the red blood-corpuscles increased before death by 10%, and in individual cases by 58%. Post mortem, increases of up to 150% were found. In animals recovering from phosgene poisoning I observed during shock decreases of hæmoglobin concentration inside the red blood-corpuscles which amounted on average to 5%, but reached 16% in extreme cases. Similar changes were found, but were

1. Cordier, D. B.M.R.C.: Report V6492 and V7294; note F590. Wojskowy, L. *J. Polish Army med. Cps*, 84.
2. Underhill, F. P. The Lethal War Gases. New Haven, 1920.
3. Scheuring, H. Z. Patologia zatrucia fosgenem (Pathology of Phosgene Poisoning). Ed. by W. Drodze. Jerusalem, 1944.

Digitized by Google

discarded, by Underhill, as is evident from protocols of his experiments. I have termed these changes in concentration and dilution of hæmoglobin inside the red blood-cells positive and negative hæmoglobin-cell reaction (HbC reaction).

The changes in hæmoglobin concentration inside the red cells are undoubtedly the most important single factor in the decreased oxygen affinity of the blood; but in shock other factors, such as changes of pH and body temperature, may influence the affinity of hæmoglobin for oxygen.

With experimental phosgene poisoning there exists a characteristic difference in the relation between HbC reaction and respiration-rate in those dogs which survive and those which die. This relation can be calculated and expressed as a correlation index according to the formula of Bravais-Pearson.[4] The index varies between +1 and −1; +1 would mean complete positive correlation, the increase in respiration-rate being invariably associated with a positive HbC reaction; −1 would mean that the increase in one of the two is invariably associated with a decrease of the other. Intermediate values between +1 and −1, expressed in decimal fractions, signify that the correlation is not complete—i.e., the change of one factor is not always associated with a parallel change in the other. Index O means that no correlation exists.

Measurements for this index were taken in my experiments immediately after poisoning, and 2 and 7 hours later. In animals which survived the poisoning the index was always negative. This suggests that the increase in respiration-rate was sufficient to overcome the impairment of oxygen exchange in the lungs caused by the poisoning. In animals which died of poisoning, the index taken immediately and 2 hours after administration of phosgene was positive. This indicates that the increase in respiration-rate is no longer sufficient to counteract the impairment in oxygen exchange caused by the more severe damage in the lungs; there is then also increased hæmoglobin concentration inside the red cells which brings about decreased oxygen affinity of the blood and thus enables an increased oxygen delivery to the tissues. By 7 hours after poisoning the index has become O. This can be explained as follows. By hyperventilation the partial oxygen pressure in the alveoli could never exceed that of the atmospheric air—150 mm. Hg. When the affinity of the blood to oxygen becomes so greatly reduced by the increased hæmoglobin concentration inside the red cells, even a partial oxygen pressure of 150 mm.Hg would be insufficient for full saturation of the hæmoglobin. In other words, further adaptation of pulmonary ventilation to the HbC reaction is ineffective and thus the correlation breaks down. This is the condition in which oxygen therapy can be life-saving by providing the means for raising the partial oxygen pressure in the alveoli sufficiently to ensure full saturation of the hæmoglobin, despite its greatly reduced affinity for oxygen. In this way oxygen therapy will maintain an adequate oxygen delivery to the tissues; and anoxia with its dangerous consequences is avoided.

Mepal Hospital, near Ely. H. Z. SCHEURING.

FEMALE CIRCUMCISION IN THE SUDAN

SIR,—I hope that the well-balanced letter, signed by five doctors, in your issue of March 26, will not lead your readers to believe that there has been any appreciable reduction in the practice of pharaonic circumcision in the northern and central Sudan.

The letter implies that, as "the pharaonic method is now illegal in the Sudan," the situation has improved; but this in fact is not so. The 1946 enactment, which made the pharaonic method illegal, legalised as a substitute a method known as "government sunna,"—a method so mild that the Sudanese say it is not circumcision at all and refuse to have anything to do with it. Can any of the signatories of the letter produce evidence of *one* authentic case of government sunna in the whole of the northern or central Sudan? I very much doubt it. It is because of this, and because of the difficulties of enforcement, that this law is generally and regretfully admitted to have failed.

It would not be necessary to examine every girl to know whether or not the more severe form of circumcision was still being practised. There are some 400 government midwives—a number rapidly increasing—who must have an accurate knowledge of the position and whose reports could be checked. Moreover there are always in hospitals for various reasons a certain number of girls—quite sufficient to obtain a reliable cross-section on the trend of affairs.

Your correspondents rebut the statement that pharaonic circumcision is spreading into areas where it was hitherto unknown. Have they read S. F. Nadel's book *The Nuba* (1947), written with the approval of the Sudan government. I refer particularly to pp. 240 (and footnote) and 480. On p. 480 Nadel says that female circumcision "is also practised by the Arab tribes in the west and south-west of Kordofan (Messirya and Humr), and has spread to their Nuba neighbours." He goes on to elaborate this statement. If it is admittedly spreading amongst one primitive people, why not amongst others.

Is it fair to say that "the husband is often powerless to stop the practice"? As an individual he may be; but cannot men band together to acknowledge that pharaonic circumcision is cruel, purposeless, and against the Mohammedan religion, and refuse to take circumcised brides?

London, S.W.1. CONSTANCE E. HUDDLESTON.

HEALTH CENTRES NOW?

SIR,—"Practitioner's" views on the health service are reminiscent of Marie Antoinette's on feeding; there is difficulty in supplying bread, so "let them eat cake." His suggestion that the doctor, who can only just get through his work (probably by skimping it) when his patients attend the surgery, will be able to do it with ease when he has to visit them appears irrational to say the least. To propose giving his bizarre theory a nation-wide trial is even more irrational. If he sincerely believes that an N.H.S. practice can be satisfactorily run on luxury lines, he should himself make the first experiment. Let him circularise his patients to the effect that he is willing to visit them whenever their convenience dictates, notwithstanding any instructions to the contrary on the medical card. After a year of this he should publish his results, giving full numerical data, which might or might not justify a wider experiment.

I note with interest his first reason against a token payment—that it is "wholly inconsistent with the intentions of the National Health Service." What are these intentions? In my simple way I had believed that the most important was to provide an efficient health service, and I do not see how token payments can adversely affect this.

He suggests that if three hours of waiting are not a deterrent, neither will a token payment be. In this he overlooks two things. There was no overcrowding in the days of private practice, so a full fee is certainly a deterrent; there is gross overcrowding now. Somewhere between one would expect to find a level of payment which caused no hardship yet at least recognised that the doctor's time is more valuable than a few cigarettes. He also overlooks the *malade imaginaire* to whom the three hours' wait is a pleasurable evening in which he can exchange symptoms with his confrères. The trouble with the full waiting-room as a deterrent is that it does not always deter the right people.

"Practitioner's" fifth point would make a resounding speech from a political platform, but does not bear close examination. Is everyone who does not take more than his contractual rights to be regarded as "considerate"? If so, the doctor is "considerate" in not stealing money from the executive council to supplement his own meagre contractual right of 16*s.* a year. Reasonable shelter and seating accommodation there must clearly be, but not for an unreasonable number of patients. No-one has suggested that a fee should be charged on top of an uncomfortable and prolonged wait: the very purpose of the suggested fee is to prevent this wait.

In his penultimate paragraph "Practitioner" has drawn an unwarranted deduction. He has presumably found that, in general, patients do not ask him to visit

4. See Dahlberg, G. Statistical Methods. London, 1940.

Digitized by Google

them for trivialities. (My experience agrees with this, but it is apparently not universal, as is shown by Drs. Robinson, Phillips, and Woodcock.[1]) From this he reasons that if visits were made to all patients there would be no trivialities. Surely it is obvious that the reason for his experience is the very instruction which he would like to remove from the medical card.

I fully agree that the doctor's wife should not have the problems of staffing and accommodating the surgery, but disagree with the contention that token payments would do nothing to solve these problems. By reducing numbers they would reduce the need for vast waiting-rooms. By increasing the doctor's remuneration they would enable him to afford both extensions to premises and adequate staff. Whoever heard of an optician's wife having to work in her husband's business? The optician has ample staff (possibly more than he needs) and ample premises because he is being paid lavishly out of public funds. I should not like "Practitioner" to think that I am totally opposed to health centres—I admit there is a great deal to be said in their favour in some cases, but their function should be to facilitate the doctor's work, not to speed the conveyor belt and make the poor devil work harder for the same pay.

"Practitioner's" "new outlook towards disease" will hardly be encouraged by tired and underpaid doctors wherever they work.

Silver End, Essex. J. W. NICHOLAS.

PERSISTENT MALARIAL INFESTATION IN FULLY MEPACRINISED TROOPS

SIR,—Mepacrine in suppressive doses is an effective schizonticide, a feeble gametocide, and without effect on sporozoites.[2] It is well recognised that benign tertian malaria may relapse for periods up to three years after the patient has left endemic zones,[3] with especial liability at six weeks and six months.[4] This long latency has been explained on the supposition that exo-erythrocytic forms of parasite exist analogous with those of avian malaria, and this explanation has lately been proved correct.[5] Parasitised men returning home from endemic zones will thus constitute a reservoir of infection in Britain, and it is not unlikely that the source of the cases of indigenous malaria reported in recent years is the returned Serviceman. That such cases do not occur in greater numbers is probably due to unfavourable climatic conditions and the feeble vector propensities of the prevailing mosquitoes in this country—e.g., *Anopheles maculipennis* var. *atroparvus*. In East Anglia and the Thames estuary, however, conditions are favourable in summer for the maturation and spread of malaria. Nor must it be forgotten that until recent years malaria was common in this country, that we have a large population of non-immunes, and that air transport constitutes an ever present danger of introducing more hostile strains of mosquito into Britain.

While serving in the Royal Air Force I thought it would be useful to compute the magnitude of this potential reservoir, and decided that a minimal estimate could be formed from the number of mepacrinised healthy Servicemen with no history of malaria who harboured parasites in their peripheral blood. On returning to this country such men would escape the blood examinations normally carried out on those with a history of overt malaria.

In late 1945 a hundred airmen were selected who fulfilled the following criteria. They had all spent at least a year in the Far East and had seen service in hyperendemic malarious zones under primitive conditions of jungle warfare. They had all been taking suppressive mepacrine (0·1 g. a day) for not less than a year and had absorbed the drug as judged, inter alia, by the pigmentation of their skin. None had had a major illness in the past year, and none gave a history of proved or "clinical" malaria. At the time of sampling they were all fit and well and had been stationed in an area of low endemicity for over three months of the cool season. They were all "due for home" within two or three months. Thick blood smears were stained (Field's) and examined for malarial parasites. Five of the hundred (5%) showed intracorpuscular parasites (*Plasmodium vivax* gametocytes).

How long the affected men would harbour their parasites I could not say; only serial blood examinations and long follow-up would elucidate this point. It is known, however, that "latent" malaria may declare itself after an incubation period of nine months under experimentally similar conditions.[6]

Indigenous malaria arising from the returned Serviceman has so far proved negligible; but, should this at some future date cease to be so, the detection and cure of even 5% of healthy "carriers" may well be considered as a rational public-health procedure.

The films were checked at the Army Malarial Research Unit, Millbank, London, by Major J. Reid and Sergeant Marra, to whom I am much indebted.

Leeds. P. D. BEDFORD.

SPECIALIST SALARIES

SIR,—Truly we live in an age where quantity overrules quality. The outbursts of criticism of the terms and conditions for general practitioners under the Act, obviously unsatisfactory to all doctors, are in direct contrast to the lack of interest in the plight of the consultants, relatively a mere handful.

Before commenting on the Minister's proposals, let me recapitulate certain basic facts:

(1) No consultant or specialist at present holding a senior post has benefited from the proposed salaries payable to trainee specialists. He has learnt his art under the old unpaid or underpaid system, conditions which he accepted in the hope of recouping the lost (financial) years when fully trained.

(2) Private practice is fast disappearing. The causes of this are the high rate of compulsory insurance levied on the erstwhile private patient, the high cost of nursing-home beds (and their scarcity), and the fact that for private beds the hospitals have now doubled and in some cases trebled their charges.

(3) Consultants are to be paid for their hospital work which they previously performed free.

(4) The free consultation in the patient's home is replaced by the domiciliary scheme.

(5) The Central Consultants and Specialists Committee of the British Medical Association is alleged to represent all the consultants and specialists in the country. It is hard, however, to see how the members of this committee are to obtain the views of their constituents. It is understood that the Royal College of Physicians is calling a general meeting to discuss the proposals, but no word has been heard of the Royal College of Surgeons, the Royal College of Obstetricians and Gynæcologists, or the Scottish corporations doing likewise. The representatives of the regions will have received proposals from the staffs of the hospitals in the regions, but these representatives (of the great majority of consultants and specialists) are very much in the minority on the committee.

Bearing in mind the above facts, I suggest that the proposals would be acceptable if adjusted in certain respects.

(1) The Spens report, accepted in principle by the Minister and profession, should be *properly* implemented. This means that the rates of remuneration should be raised to cover the 85% increase in cost of living.

(2) The fees for domiciliary visits should bear some relation to the time spent and knowledge required. The fee of £4 4s. is adequate for a patient within a hundred yards of the consultant's home, but there are not many of these. A reasonable fee should be paid according to the distance travelled in a scattered region, and allowance must also be made for the fact that a six-mile journey in London takes as long as a twenty-mile one in Devonshire.

(3) The special merit awards should be allotted purely on seniority. The jealousy and bad feeling likely to be engendered by any other system would be detrimental to the profession. Also any system requiring recognition is likely to encourage massive publication of inaccurate and useless information

1. *Brit. med. J.* 1948, ii, suppl. p. 186.
2. Memoranda on Medical Diseases in Tropical and Subtropical Areas. London, 1941.
3. Megaw, J. W. D., in Rogers and Megaw's Tropical Medicine. London, 1944.
4. *Quart. Bull. Hlth Org., L. o. N.*, June, 1933.
5. Short, H. E., Garnham, P. C. C., Malamos, B. *Brit. med. J.* 1948, i, 192. See also *Lancet*, 1948, i, 182, 783.
6. Shute, P. G. *Trans. R. Soc. trop. Med. Hyg.* 1946, 40, 189.

Digitized by Google

with the idea of catching the assessor's eye. The busy and competent consultant will never be noticed.

(4) The mileage allowance bears no relation to the costs of a car under present conditions, to the county rates paid before July 5, or to the Whitley Council scales for local authorities. It has been rumoured that members of the Coal Board receive 2*s*. 6*d*. per mile, but I cannot substantiate this and would accept correction!

(5) Why should there be a limit to the number of domiciliary visits paid for? No other trade or profession is expected to work for nothing. No doubt the Minister fears dicotomy, and the mass of honest consultants must work for nothing lest a few black sheep steal an unnecessary fee or two.

No doubt there are other criticisms, both constructive and destructive. It would be better if they were voiced now, and not, like the general practitioners', after the signature has been placed on the dotted line.

Exeter, Devon. DEREK JEFFERISS.

TUBERCULOUS ABSCESS AT THE SITE OF PENICILLIN INJECTIONS

SIR,—With reference to the observation by Dr. Forbes and Dr. St. Clair Strange (March 19) of tuberculous abscess formation following the administration of penicillin, I would like to point out that such an occurrence is by no means rare although it appears to be infrequently reported. After our original observation,[1] Dr. C. Koupernik, of Paris, told me that some seven cases were observed in France within a few months.

Whilst a hæmatogenous spread is theoretically possible it is certainly curious that in none of the 9 cases we know of could any evidence of a tuberculous focus be detected. Since freeze-drying is the best method at present available for the prolonged maintenance of virulent organisms, it is possible that some batches of penicillin powder may contain live tubercle bacilli in a dried state. Clearly nothing can be done to avoid hæmatogenous spread if this is the mode of origin, but a plea can be made for the most stringent supervision of workers who come into contact with penicillin throughout its stages of manufacture and administration.

St. George's Hospital, London, S.W.1. S. D. ELEK.

STRANGULATED HERNIA TREATED BY NATIVE ENTEROSTOMY

SIR,—An adult male African was admitted to the Colonial Hospital, Tamale, with gangrene of the right half of the scrotum and a large ragged fistula near the internal opening of the right inguinal canal. Liquid fæces poured from this fistula whenever he moved.

It was impossible to obtain a history, because the patient spoke only an obscure northern Nigerian dialect. However, we were of the opinion that the condition was about four days old; that the original cause had been a strangulated right inguinal hernia, which had interfered with the blood-supply of the scrotum, producing gangrene; and that the fistula was due to native surgery, for similar cases had been seen by both of us. Native treatment consists in plunging a red-hot arrow-head into the swelling caused by the strangulation—a simple and rapid life-saving operation, but one having a very distressing end-result because native surgery is unable to repair the fistula so created.

Through a right lower paramedian incision a loop of ileum was found adherent to the inside of the fistulous opening. It was detached easily; the gut was in two portions, but the mesentery was intact. The proximal and distal ends were trimmed and united by an end-to-end anastomosis. Sulphapyridine had been administered for twenty-four hours before the operation. Locally prepared sulphapyridine powder was liberally sprinkled into the peritoneal cavity at the end of operation, and the wound was closed. No drainage tube was inserted. The fistulous opening was left untreated, apart from an acriflavine dressing, since it was considered to be a good drainage point. Sulphapyridine was continued for four days after operation.

The only sequelæ of note were that there was no bowel evacuation for eight days, and an ascites developed (possibly due to irritation by the sulphapyridine powder) after the abdominal wound had healed, which cleared up after a single tapping. The fistulous opening in the abdominal wall closed rapidly, and the ulcerated scrotum healed in just over a month.

Of the other cases of fistula mentioned above, one was considered inoperable, and another, though successfully repaired, developed a fatal retroperitoneal abscess in the third week of convalescence.

Tamale, Northern Territories, Gold Coast. M. P. BROWNE. B. B. WADDY.

1. Ebrill, D., Elek, S. D. *Lancet*, 1946, ii, 379.

AT THE CROSS-ROADS

SIR,—Dr. Banks's article in your issue of March 26 begins with a grave mis-statement of fact. He writes: "In A.D. 597 Augustine introduced Christianity to England." When Augustine landed in England one of the first things he saw was the Anglican Church of St. Martin at Canterbury, stated by the historian Bede to have been built by the Romans between A.D. 300 and 400. In St. Martin's Church Augustine worshipped while his cathedral at Canterbury was being built. The church is still standing and in use. It is also recorded that three British bishops (of York, London, and Colonia Lodiensium) with attendant clergy attended the Council of Arles in A.D. 314, and that British bishops attended the Council of Sardica in A.D. 347 and the Council of Ariminum in A.D. 360. VERITAS.

THE UNDESCENDED TESTICLE

SIR,—May I make a few observations on some of Mr. Denis Browne's statements in his letter of March 26? He says:

1. "*That all workers on the subject have completely neglected diagnosis by examination.*" In refutation of this statement I shall quote what I wrote in 1938 in collaboration with Dr. E. F. Scowen[1]: "The physician or surgeon should be at pains to determine as far as possible the particular type of maldescent with which he has to deal, for on this depends the choice of treatment—medical, surgical, or none at all." Dr. P. M. F. Bishop[2] wrote: "The first essential for the assessment of the individual case is a careful clinical examination." In both papers the authors have stressed the importance of, and fully discussed, clinical diagnosis; but perhaps these articles have escaped Mr. Browne's notice.

2. "*That while hormone treatment claims 75% of cures, the same 75% of 'undescended testicles' descend spontaneously.*" This is a sweeping and dogmatic statement which has not yet been proved, but may quite likely be true. The first to suspect this was not Mr. Browne, but Dr. Scowen and myself when in 1935 we wrote[3]: "We feel that in a large percentage of our patients [treated successfully with chorionic gonadotrophin] spontaneous descent may have occurred by the time of puberty." However, surely the likelihood of spontaneous descent does not contra-indicate hormone therapy. It appears to me that Mr. Browne does not approve of hormone therapy under any circumstances. If this view were carried to its logical (and ridiculous) conclusion, treatment should not be applied to any condition which runs its course to spontaneous recovery. Perhaps Mr. Browne is not aware of the cruelty of small boys and the gibes which the unfortunate cryptorchid has to endure in the changing-rooms of swimming-baths and in the pavilions and boat-houses of schools. Apart from this, the longer a testicle remains undescended the more likely is the occurrence of degenerative changes in the seminiferous tubules.

3. "*That there has been a remarkable lack of mention by endocrinologists of the dangers of hormone treatment to the cells of the testes.*" I wonder whether Mr. Browne can tell us the percentage of infants born with atrophic testicles. If his view that chorionic gonadotrophin may cause testicular atrophy is correct, then the whole set-up of Nature must be wrong, for the placenta produces large amounts of the very hormone we inject; circulates through the fœtus and brings about descent of the testicles *in utero*. If it damages the cells of the testes, it is surprising that the human race has survived.

London, W.1. A. W. SPENCE.

1. Spence, A. W., Scowen, E. F. *Lancet*, 1938, ii, 983
2. Bishop, P. M. F. *Guy's Hosp. Rep.* 1945, 94, 12.
3. Spence, A. W., Scowen, E. F. *Proc. R. Soc. Med.* 1935, 28, 29.

Digitized by Google

CARDIOSPASM

SIR,—In his article of April 2, Sir Adolphe Abrahams says: "To him [the psychologist] cardiospasm symbolises an insult the patient cannot swallow." With all due respect to a great teacher, may I quote a case to prove that the psychologist may be right?

Some months ago I saw a Welsh girl who had had difficulty in swallowing solids for the past three years. Her story was as follows. The day her mother died, she was very upset and her doctor gave her a tablet to take. As she went to swallow it, "I felt as though it was going to stick in my throat. I took it out and said 'silly little tablet, I can easily swallow it,'" and she did so with some water. The next day while eating lunch she again got the same feeling that she could not swallow. This feeling got worse as the weeks and months went by. In addition she had no desire to go out or mix with people. When she came to see me she had a flask of water in her handbag that she always carried to help her swallow. She proved to be a good hypnotic subject and she was regressed to the day her mother died. I said to her, when she was open to suggestion, that she could not swallow . . . the fact that her mother died . . . the mere thought of it stuck in her throat. I elaborated on this and finally she understood why and how her trouble began. Being convinced she was cured, I gave her a bun to eat, which she ate with the greatest of ease and smiling all the while. When she was awakened she kept on eating.

I heard from her on three occasions, and she never looked back; she was completely cured.

London, W.1. A. P. MAGONET.

CANCER OF THE BREAST

SIR,—Animal experiments show that for carcinoma of the breast to develop in the mouse, it is necessary that suckling should have taken place from a mother, or foster-mother, capable of transmitting a virus-like material known as the milk factor. If mice are not so suckled carcinoma of the breast does not develop.

I am anxious to start a long-term—very long-term—investigation into this matter in the human subject, and for this purpose I wish to collect the names and addresses of female children or adults of whom it is known that they have *never suckled at a human breast*. Family doctors and obstetricians may know of such cases where, because of the death of the mother, or for other reasons, it can be *absolutely guaranteed* that the child has never consumed milk from a human source. ("Humanised milk" does not, of course, count.) If, with the permission of the appropriate person, doctors would be kind enough to forward the name, age, and address of such a child or adult, together with the name of her surviving parent or guardian in the case of a child, such an investigation could be put into operation. The card or letter should be addressed to the secretary of the mastitis clinic, Guy's Hospital, London, S.E.1.

It is hoped by this means to collect the names and addresses of a large series of females who could not have received the human "milk factor," if such exists; and the investigation would proceed as follows. On receipt of the name, the child's parent or guardian would receive the following letter.

"Dear . . ., Dr. . . . has, with your permission, sent me the name of . . . who, he assures me, has not been nursed by her mother or by a foster-mother. Doctors believe now that such children, when they grow up, may be less likely to develop serious disease of the breast than other people, and this possibility you might regard as making up for the lack of what is otherwise the best method of nursing a baby. Nevertheless, it is vitally important that this theory should be tested out, and I should be most grateful to you for your coöperation which might in the future save many lives. All that I should do is to send you, once a year, a stamped addressed post-card asking you whether there has been a change of address or whether . . . has now left home. When she grows up and leaves home, I or my successor will keep in touch with her in this way, and after explaining to her that we believe that she is *less* likely to suffer from serious breast disease than her friends, ask her whether she will reply year by year on an addressed card as to whether she is still free—as we expect—from any trouble in the breast. It is perhaps only by finding out these things, which as you will appreciate, is bound to take many years, that the problem of cancer will eventually be solved.

"If when . . . grows up, she does not wish to coöperate in this matter, she can either ignore the post-card, which, after two years without a reply, will not be sent again, or she can write and tell us not to send her any more; but I hope that she, like you, will feel that by helping in this matter she is really doing her bit, and at such small cost, to alleviate human suffering and advance knowledge."

A letter in similar vein, and with appropriate modifications, will be sent to adults.

I, Sir, can see no other way in which this matter—vital to the welfare of the human race—can be settled. That the results of this experiment cannot be seen by anyone reading these lines makes it all the more important that we should start now, and be sure of answering at least one fundamental question about human breast cancer by the year 2030.

H. J. B. ATKINS
London, S.E.1. Director of Surgery, Guy's Hospital.

SIR,—The annotation in your issue of March 12 tempts me to try to express certain perplexities which have troubled me for many years.

Harnett [1] said that "actuarially it was found that radical mastectomy gave a five-year expectation of life ranging from 91·03% of normal in stage 1 down to 68·4% of normal in stage 3b." He added that after local mastectomy alone the five-year expectation of life ranged from 97·63% of normal in stage 1, to 70% of normal in stage 3b. Of 703 patients submitted to radical mastectomy, 312 survived for five years and 22 died "without cancer." Of 133 patients submitted to local mastectomy, 52 survived for five years and 16 died "without cancer." If patients dying without cancer are omitted, we are left with 681 submitted to radical mastectomy, of whom 312, or nearly 46%, survived for five years, and 117 treated by local mastectomy, of whom 52, or just over 44%, survived.

Here, surely, is food for thought. Unfortunately, as I hope to show later, the figures are vitiated by the grouping under "local mastectomy" of 83 patients in whom the axillary lymph-nodes were also excised.

Fifty years have elapsed since Halstead introduced his radical operation. Masses of statistics have been published, but can we yet say what is the best surgical treatment in the various stages? It is disquieting to find a report in the *British Journal of Cancer* for September, 1948, based on one system of grading, and a discussion at the British Medical Association in the same year based on a different system. They agree that in stage 1 the tumour is confined to the breast only, but is the absence of axillary metastases to be decided by clinical examination, or on histological examination of an odd suspicious gland, or on a thorough and painstaking search by a morbid anatomist? If only a local mastectomy is performed, who can say that no secondary glands are present? Every early stage-2 case which is grouped as stage 1 must tend to impair the survival-rate in both groups.

The surgeon who fails to perform the widest possible operation in cases deemed operable may be regarded as a heretic; yet in spite of an occasional success, my experience has been that a radical operation in a relatively advanced case appears often to shorten the life of the patient. It seems that operative measures today tend to be less heroic than those of our fathers. Sir Cecil Wakeley [2] admits to performing only a local mastectomy in cases where the breast is small and the tumour in an inner quadrant. Here one may note with interest that Harnett finds that the situation of the tumour has little bearing on the prognosis. Everyone is agreed that the radical operation gives reasonably good results in stage-1 cases; yet at the B.M.A. discussion the ten-year survival-rates recorded by recognised experts varied from 65% to 91%. So variable are the manifestations of this dire disease that the statistical results of individual operators are of limited value.

In a long surgical career I have operated on several hundred cases of cancer of the breast. With difficulty

1. Harnett, W. L. *Brit. J. Cancer*, 1948, 2, 212.
2. Wakeley, C. *Brit. med. J.* 1948, ii, 631.

Digitized by Google

I found the time to follow up rather over 150 for periods varying from five to ten years. Taking courage from the results, I have gradually tended to abandon the classical radical operation for one which conserves the muscles. That is to say, I excise an adequate amount of skin centring on the tumour and a wide area of fascia. I clear the axilla as thoroughly as firm retraction of the pectorals will allow. The patient is left with unmutilated muscles, but the operation is in no sense a local mastectomy. I regret that I have not followed up more patients but the results are as follows:

Of 40 stage-1 cases, I performed what I may term the modified operation in 37; and 29 (78%) have survived between five and ten years. Of 115 stage-2 cases (B.M.A. grading) I did radical operations in 42, with 27% of the patients surviving between five and ten years, and 73 modified operations with 42% surviving.

Granting that there was a tendency to perform the radical operation in the more advanced cases, the combined survival-rate of 36% is still an improvement on some published figures. The so-called radical operation has been accepted without question by the great majority of surgeons because it appears to have a scientific basis. But until we know more about the natural defences of the body, it is rash to assume that the prospect of cure increases with the extent of the ablation. What is it that causes the disease to recur in a patient apparently cured for many years? The invading cancer cells must have been imprisoned but not eradicated. How have the guards been overthrown? Many years must pass before the results of any modification of surgical treatment can be assessed. To stray from the path of orthodoxy may prejudice the chances of the individual patient.

The development and progress of cancer in the mouse is proportionate to its brief span of life. Has anyone ever experimented with operative surgery in mammary cancer in the mouse?

There are so many conflicting views on X-ray treatment that it is difficult to assess its value. The limitation of surgery suggested by the striking figures of McWhirter[3] awaits confirmation.

Northampton. C. C. HOLMAN.

Parliament

Red Cross Aid For Arab Refugees

IN the House of Lords on March 29 the ARCHBISHOP OF YORK called attention to the condition of the Palestinian refugees. He said that massacre in Palestine had been followed by a panic-stricken exodus from their homes of Arabs now believed to number about 800,000. Of these people 200,000 were living in caves and beneath wattle shelters; more than 50,000 in catacombs under an amphitheatre; thousands more in holes which they had dug in the ground. Where tents were available they had been occupied by 50 persons instead of the 10 for whom they were intended. They had little food or clothing; disease was rife among them. Smallpox, dysentery, and other diseases had spread, and it had been stated on good authority that in one district 220 women and children were dying every day. Efforts had been made by the Church Missionary Society, the Orthodox Church, the Roman Catholics, the Quakers, and the British Red Cross to relieve the situation by medical and other aid, but it was recognised that they were inadequate to meet the problem. The United Nations had voted considerable sums of money to which Great Britain had promised to contribute £1 million. Could some of this money—say £75,000—be placed at the disposal of the British Red Cross? But it would be breaking every law of justice if the United Nations accepted the position that these people must be permanently excluded from their homes. It would be well for the stability of Israel, while there was time, to show a conciliatory attitude to these refugees.

Lord AMULREE, speaking from the point of view of the Red Cross, urged the need for prompt help. He supported the plea that some of the money which the British Government had already put down should be given direct to the Red Cross, who did their work in the field. The refugees in Transjordan had been assigned to the care of the British Red Cross by the International League of Red Cross Societies. But he was fearful that if there was not a direct allocation the money would be caught up in the bureaucratic whirl, and some time would elapse before it was released for helping the people for whom it was intended. The refugees died of starvation and disease because there were no drugs with which to treat them. They were afflicted with dysentery, malaria, smallpox, beriberi, and wasting diseases connected with gradual starvation. The British Red Cross authorities had done as much as they could. They had established one small hospital, which was already overcrowded, and they had several dispensaries going in some of the biggest refugee camps. But the British Red Cross needed money more than anything else to buy drugs and food.

Lord HENDERSON, parliamentary under-secretary of State for foreign affairs, said that this, the most recent refugee problem, was pitiable and tragic. H.M. Government had taken the initiative both in action by themselves and in pressing for action by others. They were all proud to know that the British Red Cross and other voluntary British societies were among the first in the field, and that the total British contribution of £1 million to the United Nations' scheme was the first substantial sum on which Mr. Griffis, American Ambassador in Cairo, and Sir Ralph Cilento, director of the United Nations Relief Organisation, were able to draw. Discussions were now going on between the United Nations, the League of Red Cross Societies, and the British Red Cross to see how far the funds required by the British Red Cross could be made available to them. It was also good news that the United States government's contribution of 16 million dollars had been passed by Congress. Mr. Griffis estimated that on present contributions he should be able to continue feeding the refugees until December. The refugees in the Gaza area were being fed on a scale of about 2000 calories a day, and they were being sheltered. While Lord Henderson had no precise information about the refugees in other parts, he understood that feeding was on a reasonable level and that shelter of some sort had now been provided, but the relief funds did not stretch to the provision of useful work or even recreation. The British Government would take every opportunity to encourage United Nations' relief work, but they realised that the more serious problem of resettlement remained unsolved. They would be glad to give encouragement and advice for the resettlement of the refugees and were anxious to see practical plans produced.

QUESTION TIME

Provision of Analgesic Apparatus

Lady TWEEDSMUIR asked the Minister of Health at what date he asked the Medical Research Council to solve, as quickly as possible, the problem of finding a safe and effective analgesic agent for midwifery, and to devise for its administration apparatus that is light, simple, and requires, a minimum of maintenance.—Mr. A. BEVAN replied: There was no need for me to make that request because the Medical Research Council, as I was aware, took into consideration the recommendation made in this matter by the working party on midwives, and they have decided to set up a committee in accordance with that recommendation. Lady TWEEDSMUIR: Can the Minister tell the House what stage the researches have now reached, and can he also give an assurance that he will press forward with the provision of transport and the present forms of analgesia in all districts, and not wait until new forms are known?—Mr. BEVAN: The hon. Lady knows that there is a very considerable change taking place in this field. A lot of alterations are being made in the apparatus, and I am hoping that before very long very much cheaper and more easily transportable apparatus will be produced. However, that will not be allowed to interfere with the provision of transport for midwives, which is proceeding at a much accelerated rate.

Mr. PETER THORNEYCROFT: Is the Minister aware that some local authorities are using as an excuse for not providing

3. McWhirter, R. *Proc. R. Soc. Med.* 1948, 41, 122.

Digitized by Google

any additional apparatus, or any apparatus at all, the possibility that at some unknown date new apparatus will become available, and will he make it perfectly plain that they must not delay providing apparatus on that account?—Mr. BEVAN: I think it is true that some local authorities might be tempted to postpone the use of this apparatus in the hope that a lighter one will be available. I have impressed upon them that they must not allow that consideration to influence them, and we are making very considerable progress in the provision of the apparatus.

Mr. THORNEYCROFT asked the Minister which were the 11 local health authority areas in which no analgesia is being used in the domiciliary midwifery service.—Mr. BEVAN: The number of county and county-borough councils in question is now eight. They are:

Name of county or county borough	Number of domiciliary midwives qualified to administer gas-and-air analgesia	Position as to gas-and-air apparatus
Merioneth county	4	3 sets on order
Bath county borough	3	1 set available. Ministry in touch with council
Burnley county borough	8	4 sets being ordered
Chester county borough	0, but first one now in training	Ministry in touch with council on aquisition
Dudley county borough	10	ditto.
Merthyr Tydfil county borough	1	5 sets on order
Nottingham county borough	11	6 sets of apparatus now obtained: further sets to be acquired. Ministry in touch with council
St. Helens county borough	6	Ministry in touch with council on acquisition

Mr. THORNEYCROFT: If the Minister claims that he has power to impose this duty on local authorities, what has he been doing?—Mr. BEVAN: The answer is—more in three months than was done in five years by the party opposite.

Lady TWEEDSMUIR: Is the Minister aware that, as this fight for the provision of analgesia for every mother in the country has been a fight against the prejudice of the entire community, it is quite unnecessary to make party political points?—Mr. BEVAN: I am indeed happy to hear that there is no desire to make party prejudice and capital out of this matter, but the fact is that if there is any prejudice against analgesia it is on the side of the party opposite and not on this side.

Dr. S. SEGAL asked the Minister what was the lowest cost of apparatus for the administration of 'Trilene' analgesia in obstetrics; whether he was satisfied that it is sufficiently portable; and whether any areas would now be designated as trial areas for intensive scientific investigation into the suitability of this apparatus for use by midwives in domiciliary cases.—Mr. BEVAN: There are several types of apparatus all of which are portable. I understand that the lowest price of the types on the market is about £7. The suitability of existing apparatus for use by midwives in domiciliary cases will, no doubt, be among the matters investigated by the expert committee appointed by the Medical Research Council. Dr. SEGAL: In view of the very low cost of this particular apparatus and that it is easily portable, would it not be advisable to equip every midwife with this trilene apparatus and encourage her to use it wherever possible?—Mr. BEVAN: I understand that it is not yet certain that it is safe for midwives to use the trilene apparatus without assistance, and I certainly would not advise this course.

Mrs. JEAN MANN: Is the Minister aware that trilene is usually conceded to be the most popular, the most simple, and the most easily transportable analgesic and that its use by midwives has been prohibited by the Royal College of Obstetricians and Gynæcologists; and in those circumstances does he feel it advisable that he should counter a decision which has obviously been taken in the interest of the mothers themselves?—Mr. BEVAN: I have already pointed out that I think it is undesirable for this analgesia to be given without assistance. I mean by that without specialised assistance, and I certainly would not override the technical advice given by the Royal College.

Analgesia in Scotland

Lady TWEEDSMUIR asked the Secretary of State for Scotland how many women received analgesia in childbirth in their own homes in the city and county of Aberdeenshire, respectively, in the years 1947 and 1948, who were attended by midwives only.—Mr. ARTHUR WOODBURN replied: No apparatus was available in Aberdeen city in either of these two years. Four sets were available in the county towards the end of 1948 and 12 women received analgesia when attended by midwives alone in their own homes.

Mr. PETER THORNEYCROFT: Is this not a disgracefully low average; and might I ask what orders the Minister has issued to the local health authorities on this matter, and under what section of what Act he has issued those orders?—Mr. WOODBURN: If the hon gentleman knew Scottish health authorities he would know that issuing orders was not the way to get their coöperation. A second point is that Aberdeen refrained from purchasing this apparatus in the belief that a more efficient or a more economical apparatus was coming along shortly—and that is quite a good Aberdeen reason.

Lady TWEEDSMUIR: Will the Secretary of State tell the House whether, in fact, he has power to impose a duty upon local health authorities in Scotland?—Mr. WOODBURN: Aberdeen is now awaiting delivery of the apparatus.

Doctors' Lists

Mr. A. C. BOSSOM asked the Minister of Health what estimate he had made for the purposes of the National Health Service of the number of patients which a doctor may reasonably be expected to see in a day or an hour.—Mr. BEVAN replied: The number of patients whom a doctor can attend varies according to the circumstances of his practice and no precise estimate is possible. Mr. BOSSOM: Does not the Minister realise that certain doctors today are having a great number of patients whom they have to try to look after in an hour, and that the point of my question was how many the Minister himself expected a doctor to look after in the space of one hour?—Mr. BEVAN: Obviously, the hon. Member ought to realise that the number of patients whom a doctor can attend to in an hour depends upon the physical condition of the patients whom he is seeing. Some patients require more time than others, and in some parts of the country, where the age of the population is higher, a higher percentage of people will need to see the doctor, so that it really is not possible to make a generalisation of the kind which the hon. Member desires.

Supplies of Streptomycin

Mr. GRANVILLE SHARP asked the Minister what progress had been made in the production of streptomycin; and what increase there had been since July, 1948, in the number of hospitals where streptomycin treatment is normally available.—Mr. BEVAN replied: Production is now sufficient to cover all medical needs for which the use of the drug is reliably indicated and to provide small but increasing quantities for export. Further expansion is planned. Since July, 1948, the number of hospitals in England and Wales where streptomycin treatment is available has been increased from 30 to 220.

Emergency Beds

Dr. SEGAL asked the Minister whether he would arrange for at least 1 bed for the admission of emergency cases to be reserved nightly in all hospitals of over 200 beds.—Mr. BEVAN replied: No, Sir. Hospitals normally reserve the number of beds shown by experience to be needed, and in emergency put up extra beds. Dr. SEGAL: Is the Minister aware that there is a great deficiency of beds for acute emergency cases and many lives have been endangered through lack of these facilities?—Mr. BEVAN: It is certainly true that there is more demand for beds today than there was before, and that there are many more beds to meet the demand. What is now happening is that we are hearing of these cases where formerly we did not.

Sir HENRY MORRIS-JONES: Is it not the case that before this Act came into force no hospital in London, or anywhere else, refused emergency sick cases? Now that it is the Minister's responsibility, is he aware that, in London particularly, medical men are harassed and have to be on the telephone for over an hour every day trying to get sick people into hospital, and will he go into the whole matter again?—Mr. BEVAN: The hon. Gentleman is inaccurate in his statement. It was often very difficult to get emergency

Digitized by Google

cases into hospital. What is now happening is that there is fixed responsibility for this whereas formerly responsibility was diffused and no-one knew about the complaints.

Hospital Waiting-lists

Mr. C. S. TAYLOR asked the Minister whether he would call for a return from all hospitals of the waiting-list for admission by patients; and whether he would consider publishing, for the benefit of medical practitioners, a list of hospitals where it is known that facilities for early admission are available.—Mr. BEVAN replied: A review has just been made, and an annual return will be obtained in future. The whole matter is being studied by my standing medical advisory committee.

Architects for Regional Hospital Boards

Mr. G. M. SHARP asked the Minister how many regional hospital boards had appointed full-time architects; how many others had invited applications for such appointments; for what reasons these were justified; and, in particular, whether the work of the regional architect was advisory or executive in character and included work initiated by hospital management committees under the board.—Mr. BEVAN replied: 12 regional hospital boards have appointed full-time architects. Of the remaining 2, neither has yet invited applications for such appointments. The regional boards are responsible for all capital works of construction, reconstruction, and adaptation at non-teaching hospitals, and also for the supervision of major schemes of building maintenance. The majority have found that this necessitates the employment of full-time professional officers. The work of the regional architect may be both advisory and executive and include the handling of proposals designed to meet needs made known to the boards by hospital management committees.

Spa Treatment

Colonel M. STODDART-SCOTT asked the Minister if he would make available under the health service outpatient spa treatment to patients of other hospitals than the spa hospitals when such treatment has been advised by the specialist.—Mr. BEVAN replied: I am advised that spa treatment should only be given under the supervision of the appropriate specialist at the spa hospital. Colonel STODDART-SCOTT: Is the Minister aware that there is a large number of people waiting for spa treatment, that spa hospitals are full, and that this treatment has been recommended by specialists who are capable of prescribing it, and could not he do something to make this treatment available to the people requiring it without their having to go to the special hospitals?—Mr. BEVAN: I understand that the question is about special treatment and special hospitals. If the hon. and gallant Member has treatment for rheumatism in mind at other hospitals, that is now provided under specialist care.

Psychiatric Treatment for Prisoners

Mr. LYALL WILKES asked the Home Secretary what was the number of psychiatrists employed full-time within the prison service; the number of prison doctors who possessed special psychiatric qualifications; the number of prison inmates at present serving sentences for homosexual offences; the number or percentage of such prisoners who had received psychiatric treatment at the latest convenient date; and what steps were being taken to improve the position.—Mr. CHUTER EDE replied: No psychiatrists are employed full-time in the prison service but 6 are engaged in a part-time capacity; 5 prison medical officers possess special psychiatric qualifications, and many others have mental hospital experience. There are 412 prisoners now serving sentences for homosexual offences. Prisoners convicted of these offences who in the opinion of the medical officer may benefit by psychiatric treatment are transferred to the prisons at which there are psychiatric clinics if their sentences are long enough. During the past six months, 40 homosexual offenders have received psychiatric treatment at these centres, and of those at present under sentence 35 additional cases have received psychiatric examination and guidance at other prisons. Arrangements have also been made, from which prisoners convicted of these offences will benefit, to extend the psychiatric service available for prisoners who may benefit from treatment but cannot be removed to the special centres. Research, partly therapeutic in character, into the psychological and endocrinological aspects of homosexuality is being conducted at two selected prisons, and homosexuals will also benefit from research which is in progress into psychopathic personalities.

Public Health

Fluorosis at Fort William

IN 1945 the Medical Research Council appointed a Fluorosis Committee "to determine any effects of exposure to fluorine compounds on workers employed in factories manufacturing aluminium in Inverness-shire by an electrolytic process and also to determine any similar effects upon those living in the neighbourhood of such factories." The results of a comprehensive investigation have lately been published.[1]

In the Western Highlands of Scotland are two aluminium factories, one at Fort William and the other at Kinlochleven, and the investigators devoted their attention mainly to the conditions in and around the Fort William factory. In 1943 it had been reported that sheep and cattle nearby had been suffering from an unusual form of wasting, despite abundance of grass, and that the teeth of some of the school-children in the area were becoming mottled. The smoke from the factory chimneys was found to contain substantial quantities of fluorine arising from cryolite which is used as a flux in the manufacture of aluminium.

As regards the livestock, Prof. G. F. Boddie had reported in 1943 that their poor condition was due to dental abnormalities which prevented proper chewing of the cud, their teeth showing changes which could be ascribed to excessive intake of fluorine. Analyses of the teeth and grass had revealed large quantities of fluorine, but the water in the burns was not contaminated. In 1944 Dr. A. M. Frazer, medical officer of health for Inverness-shire, raised the question of possible effects on human health from pollution of the atmosphere at Fort William, and Mr. E. A. Birse, Chief Alkali Inspector for Scotland, reported on the fluorine escaping from the factory smokestacks. Both had noted that the trees to the north of the factory had a blighted appearance.

The clinical and environmental parts of the investigation were undertaken by the staff of the Department for Research in Industrial Medicine at the London Hospital, under Dr. Donald Hunter; Mr. J. H. T. Douglas of the Department of Health for Scotland, made the dental examinations, and Professor Boddie continued his work on the effects of fluorine compounds on animals in the area. Prof. G. H. Bell and Dr. J. B. de V. Weir examined bones from affected sheep with reference to their breaking-stresses in relation to structure. Professor Boddie also explored the possibility that the wasting of the cows and sheep might be due to a deficiency of cobalt in the diet.

In one of the factory furnace-rooms, where conditions were worst, atmospheric concentrations of fluorine as high as 3·60 mg. per cubic metre were found. Outside the factory the fluorine concentrations were much lower, being about 15% of average furnace-room concentrations at 200 yards but about 3% at some points a mile from the factory. Samples of soil and grass collected over a wide area showed contamination with fluorine varying to a large extent with geographical and climatic factors. Samples of dried soil collected in the immediate vicinity of the factory had a high fluorine content, of the order of 1010 parts per million. At right-angles to the prevailing wind there were 13 parts per million 3·3 miles from the factory, whereas in the direction of the prevailing wind the concentrations were higher; 66 parts per million were found as far as 7 miles from the factory. Samples of fresh water from various sources in the area were found to have low fluorine contents, the highest being 0·18 parts per million.

1. Industrial Fluorosis: A study of the hazard to man and animals near Fort William, Scotland. A report to the Fluorosis Committee by John N. Agate, G. H. Bell, G. F. Boddie, R. G. Bowler, Monamy Buckell, E. A. Cheeseman, T. H. J. Douglas, H. A. Druett, Jessie Garrad, Donald Hunter, K. M. A. Perry, J. D. Richardson, and J. B. de V. Weir. Medical Research Council M.R.C. Memo. no. 22. London: H.M. Stationery Office. 1949. Pp. 131. 4s.

Digitized by Google

In the clinical examinations few disabling symptoms were encountered. Hæmoglobin levels and blood-counts fell within normal limits, and the amounts of fluorine excreted in the urine varied from 9·03 mg. in 24 hours in furnace-room workers to 0·45 mg. in school-children. In 56 cases out of 437 the X-ray appearances of the bones were abnormal, but only a few were diagnosed as having fluorine osteosclerosis. Despite these bone changes none of the workers was found to be disabled. Amongst the older furnace-room workers examined, the incidence of X-ray abnormality was found to increase with increasing length of exposure to factory fumes. A possible criticism of the report of the clinical examinations is that it is overlaid with a statistical pattern of thought and is perhaps less interesting to the clinician on that account. The statistical method ignores the illuminating case or cases, and the observed/expected ratio, though undoubtedly valuable, tends to arrest or retard full clinical understanding. Again, it is hard to understand why sampling of a small factory population should present a truer picture of conditions than examination of the whole population.

Mottling of the teeth was found in 21 school-children out of 373 examined (5·6%). In two other series away from the Fort William area 3·1 and 0·6% had mottling.

The extended examinations of the cattle and sheep confirm the earlier conclusions that the wasting was due to the abnormal condition of the teeth. The incisors showed mottling of the enamel, with distortion and deformity. In the cheek teeth, by a process of selective abrasion, long sharp points formed, which pressed into the gum of the opposing jaw; and the interlocking of these prolongations prevented the animal from chewing its food properly. The wasting from which the animals were suffering was, therefore, primarily mechanical and not toxic. The fluorine contamination of the herbage seriously affects sheep and cattle farming in the area, and this is perhaps the main practical point brought out by the report. It becomes obvious that the amount of fluorine discharged from the factory should be greatly reduced. The effect of fluorine both on the factory workers and on the surrounding population is less than might have been expected.

The report, which is attractively presented, contains an extensive bibliography and discussion of previous work on fluorine, but makes no reference to Wilkie's description [2] of the first two cases of fluorine osteosclerosis to be found in this country.

Statistics for 1948

Provisional figures given by the Registrar-General [3] show that in England and Wales in 1948 the general death-rate was 10·8 per 1000 total population, compared with 12·0 in the previous year and the previous lowest of 11·4 in 1930 and 1945. The infant-mortality rate was 34 per 1000 related live births; this is the first time the annual rate has fallen below 40 and is an improvement of 7 per 1000 on the previous lowest in 1947. Some countries, however, still have lower rates; for example, the provisional 1947 rate for Sweden was 25. The proportion of stillbirths to total births was 23·1 per 1000 —1·0 lower than the best previous figure, which was also attained in 1947.

There was a fall in the birth-rate from 20·6 per 1000 total population in 1947 to 17·9 in 1948, but the effective reproduction rate (provisional) is still above par.

The total population of England and Wales at June 30, 1948, is given as 43,502,000 (males 21,091,000 and females 22,411,000) and the civilian population as 42,750,000 (males 20,370,000 and females 22,380,000). Projections of the total population of England and Wales by sex and age to mid-1950 and mid-1960 give the total population at those dates as 43,685,000 and 44,906,000 respectively. These projections are, of course, made upon certain assumptions—for example, that births will be at the rate of 700,000 per annum to mid-1955 and at the rate of 650,000 thereafter.

The fourth quarter.—There were 179,680 births registered during the December quarter, representing a birth-rate of 16·4 per 1000 total population. The number of illegitimate births was 8879, or 4·9% of the total births registered. Stillbirths numbered 4206, representing a rate of 22·9 per 1000 total births. The 125,557 deaths registered in the quarter represent a death-rate of 11·5 per 1000 population. Deaths of children under one year of age numbered 6473, representing a provisional infant-mortality rate of 35 per 1000 related live births.

Survey of Sickness.—Out of 2671 men interviewed, 1498 reported some illness or injury in August and there were 857 consultations with doctors; out of 3238 women interviewed, 2232 reported some illness or injury in the same month and there were 1270 consultations with doctors. Illness or injury of some kind during a month during July, August, or September was reported by 64·4% of all persons interviewed; the average incapacity was 0·8 of a day per month. Among housewives 72·4% reported having had some illness or injury during a month, compared with the general level of 64·4%.

SCOTLAND

Reviewing 1948, the Department of Health for Scotland [4] reports that infant mortality was the lowest ever recorded (44·7 per 1000 live births); maternal mortality fell to a new low figure (1·5 per 1000 total births); and the general death-rate also reached a new low figure (11·8 per 1000). Other items listed on the credit side are a record low stillbirth rate (28·7 per 1000 births); a sharp decline in neonatal mortality (25·1 per 1000 live births); a continued improvement in the incidence of, and death-rates from, infectious diseases, with the sole exception of tuberculosis; and the continued success of the diphtheria immunisation campaign.

There were few important outbreaks of infectious disease. Deaths from diphtheria numbered only 31, compared with 488 in 1928 and 430 in 1938. The death-rate from tuberculosis, however, showed very little change over the whole year. The death-rate from respiratory tuberculosis—66 per 100,000 population—was the same as in 1947; provisional notifications numbered 8010 as compared with 7984. Notifications, the report points out, have increased year by year since 1939 when they numbered 4657: "It is necessary to go back to 1921 to find a figure comparable with that for 1948." The non-respiratory tuberculosis figures were, however, better; notifications at 1877 were about 250 fewer than in 1947. The number of deaths was 486 (9 per 100,000 population) as against 707 (14 per 100,000) in the previous year.

More blood than ever before was used for transfusion in Scottish hospitals. To meet the demand, approximately 40,000 volunteer blood-donors contributed; but there is need for 10,000 new donors every year to ensure maintenance of this service.

The National Health Service came into existence without serious dislocation, states the report, having regard to the administrative problems involved.

> "The two main difficulties so far have been scarcity of staff and restrictions on building. For the general practitioner services there were barely enough doctors and not enough dentists; for local authority health services there were insufficient health visitors to cope with extended duties, a scarcity of assistant medical officers of health and a great dearth of dental officers; and in hospitals the shortage of nursing staff was serious. These difficulties made it inevitable that for a time the Service be carried on with very little increase in its total resources."

The two main changes to be looked for—coördination of the services, and improvement and development in the areas with inferior services—are matters of long-term planning. "All that can be said now is that the Service promises well."

2. Wilkie, J. *Brit. J. Radiol.* 1940, 13, 213.
3. Registrar-General's Return for the Quarter ended Dec. 31, 1948. H.M. Stationery Office. Pp. 25. 1*s.*
4. Report of the Department of Health of Scotland for the year 1948. H.M. Stationery Office. Pp. 88. 1*s.* 6*d.*

Digitized by Google

The fourth quarter.—The Registrar-General for Scotland[5] reports the following figures for this quarter: birth-rate 18·5 per 1000; death-rate 12·2 per 1000; maternal-mortality rate 1·1 per 1000 total births; infant-mortality rate 44 per 1000 live births; and death-rate from tuberculosis 74 per 100,000—a slight improvement on the rate for the corresponding quarter of 1947, due to a decrease in deaths from non-respiratory tuberculosis.

B.C.G. Trials

At the end of last year the Minister of Health announced that arrangements for the trial use of B.C.G. vaccine against tuberculosis in this country were nearing completion.[6] On March 29 Edinburgh health committee decided to ask the Department of Health for Scotland for permission to make the first large-scale trial in their city. Dr. W. G. Clark, the medical officer of health, has suggested that in the first instance two classes of the community should be protected—children who are members of an infected household, and nurses and students coming into contact with tuberculosis.

Smallpox

A passenger, aged 69, who became ill about March 21 on board S.S. *Mooltan*, during a voyage from Australia, died at sea on April 1. The fatal illness, at first believed to be chickenpox, was later found to be smallpox. The ship arrived in the port of London on April 2 with 953 passengers and 441 crew. All except two were either vaccinated or revaccinated before leaving the ship on April 3. Local health authorities are being advised of the names of these people and of the addresses to which they have gone; also of the names and addresses of a number of persons coming to the United Kingdom who left the ship at Marseilles, without being vaccinated, on March 25. The wife of the passenger who died was taken ill on April 3 and has been removed to a smallpox hospital.

Passengers and crew on this ship were at risk of being infected by smallpox for about a week before they were vaccinated or revaccinated on April 3. The vaccination of contacts after exposure to infection cannot be relied upon to afford complete protection, and there is a definite likelihood that further secondary cases may occur during the next fortnight. Medical practitioners called to see any passenger or member of the crew from the S.S. *Mooltan* during the next few weeks are requested to consider carefully the possibility of smallpox, and if in doubt to inform the local medical officer of health, who will be prepared, if necessary, to obtain the advice of a consultant.

Influenza

Deaths from influenza in the great towns of England and Wales in the week ended March 26 numbered 327, compared with 360 in the previous week; the only area in which the number of deaths increased was the Midlands. Most of the deaths were in old people.

5. Quarterly Return of the Registrar-General, Scotland, for the Quarter ended Dec. 31, 1948. Pp. 29. 1*s.*
6. *Lancet*, 1948, ii, 911.

Notification of Infectious Diseases

ENGLAND AND WALES

—	Week ended March			
	5	12	19	26*
Cerebrospinal fever	33	35	57	39
Diphtheria	101	101	114	117
Dysentery	65	49	35	34
Encephalitis lethargica	2	1	..	1
Food-poisoning	94	15	17	15
Measles, excluding rubella	18,659	17,306	16,275	15,307
Ophthalmia neonatorum	34	34	56	47
Paratyphoid fever	5	3	2	7
Pneumonia, primary or influenzal	1500	1514	1524	1547
Polioencephalitis	1	3	..	2
Poliomyelitis	9	17	18	15
Puerperal pyrexia	106	95	104	99
Scarlet fever	1190	1178	1214	1357
Smallpox	..	..	..	..
Typhoid fever	4	1	3	3
Whooping-cough	2653	2625	2793	2978

* Unrevised figures.

Obituary

PHILIP BRUCE WHITE

B.SC. WALES, F.R.S.

Philip Bruce White, bacteriologist at the National Institute for Medical Research, died on March 19 at the age of 57, after an illness of some months' duration.

The son of Philip J. White, the first professor of zoology at University College, Bangor, his childhood was spent at Bangor, and he graduated there in zoology and botany. His earliest publications suggested he was set for a conventional career as a zoologist, but the 1914 war diverted his attention to bacteriology. He became assistant pathologist at Trinity College, Dublin, in 1915, and civilian pathologist to the Army Laboratory at Tidworth the following year. In 1919 he went to Aberdeen, where his first important discovery was the proof that the causal agent of Isle of Wight disease of bees was a mite, parasitic in the trachea.

But his real life-work began when he joined W. G. Savage at Bristol and started a long series of investigations into the ætiology of food-poisoning. One of his more spectacular researches there was the demonstration of the presence of botulinus toxin and organisms in the wild-duck paste which killed eight people who ate it at a picnic at Loch Maree. He brought order into the classification of the salmonellæ associated with food-poisoning, and the methods which he established for dealing with these groups of organisms became the foundation of future developments in bacteriological analysis. He continued this work when he transferred for a short time to the Lister Institute, and in 1927 to the National Institute for Medical Research where he remained for the rest of his working life. There the angle of his approach altered slightly and he became increasingly interested in the isolation of the various specific antigens which characterise races and species of bacteria.

In 1933 he turned most of his attention to cholera, and with comparatively simple techniques made great advances in the study of the antigenic make-up, and differentiation, of strains of cholera vibrios. The late war interrupted these investigations, for he was engaged on confidential work for the Government; but he eventually found time for researches on gas-gangrene and anthrax. He had returned to his cholera work when he was taken ill, and it is probably for these studies that he will be remembered in scientific circles. His reputation was international, and he was called for consultation to India in 1946 and to Egypt in 1947.

A good deal of White's time at the National Institute was occupied with the routine work of the department of biological standards, and he was a great support to the director on the bacteriological side of the work. One of the most laborious jobs he undertook in this connexion was the checking of the potency of all the batches of penicillin manufactured in this country for about twelve months towards the end of the war. He worked literally night and day at this drudgery, doing the major part with his own hands. Characteristically he devised his own method of assay, which probably has the lowest intrinsic error of any of the many biological methods.

A colleague, to whom we are indebted for this memoir, adds: "Bruce White was a good example of a successful transference from one scientific discipline to another. He had little or no formal training as a bacteriologist, but became a leading authority on the subject. Nor did he remain a taxonomist, as might have been expected from a zoologist; although he never lost his appreciation of the importance of taxonomy, he was always probing into the fundamental basis of taxonomic differentiation. His technique was simple but elegant; his results inspired confidence.

"Outside his work, he had wide interests. An excellent French linguist, he could make himself understood in three or four other languages. He was a lover of French poetry and had some poetic gift himself; and with his excellent draughtsmanship went a talent for caricature which suited his puckish humour. He left a wife and two sons, both of whom had taken up medicine. It was obviously a great joy to him in his last illness that already the older of his sons had started work in his own field."

Digitized by Google

Notes and News

LIVING IN COMMUNITIES

NEIGHBOURHOODS vary as much as people. A friendly pattern is common in some villages, while others pride themselves on their unsociability. Both types of behaviour have drawbacks and advantages, and both owe much to local custom and tradition. P.E.P., investigating the community spirit, have lately asked "Can Communities be Planned?"[1] In the intimate local life of a village, they say, "everyone knows everyone else, joins keenly in social activities and takes part in running village affairs." This is true, anyhow of some villages; but it carries with it some well-known thorns, notably lack of privacy, intolerance, and a deal of gossip. Recognising this, P.E.P. pause to consider whether, in our current attempts to revive community life based on places, we are moving against people's wishes. But there is good evidence that many people, especially in towns, are lonely and friendless. Young women at the Peckham Health Centre, it seems, often say "I hadn't a friend before I joined the Centre." The success of clubs for old people shows how the aged long for company. In new housing estates delinquency is prevalent among young people, often for lack of common and constructive enterprises. Moreover, since democracy is rooted in personal responsibility, a place with a vigorous community life is likely to take its civic and political duties seriously. Recent studies suggest that a higher proportion of people vote in small places than in large, and it may be that responsible citizenship thrives best among groups of people small enough to know one another well and to understand their common interests. Pride in a local football team is not so different from pride in local community services. Some measure of community spirit is to be found in difference of response to outside appeals: some reception areas during the war took great pains to settle the children sent there, while others remained hostile and indifferent. On the whole it seems the benefits of a good community spirit outweigh its drawbacks, both for the community and for its neighbours.

In new communities—new housing estates, satellite towns, development areas—large numbers of people are often moved into new houses at the same moment and community life has to start from scratch, with no local institutions to mould it. Schools and community centres should probably be built early, for these are a focus of common interests. Nevertheless community spirit often develops best in an atmosphere of makeshift: squatters living in squalid conditions are often rich in it, partly no doubt because they have plenty of opponents in common. Residents' associations in new areas are often lively while they still have something to fight for—new schools, safer crossings, more convenient bus stops—but lose their fire once such problems have been solved. When a group of people are moved to a new housing estate, as sometimes happens in slum clearance, they bring the old ties, but sometimes too the old bad habits; and for this reason, in some estates large groups from the cleared areas have been deliberately broken up. P.E.P. suggest that if group colonisation is encouraged, the settlers could be organised into associations during the waiting period, and could come to their new housing estate, or their new town, with their community loyalty already established. Families should be encouraged to bring their kin to live within easy visiting distance, for visiting kindred, P.E.P. find, is "a major social occupation" in this country. Children of existing tenants might be given preference when houses are allocated, and houses suitable for old people should be a part of every estate. Community feeling is also encouraged when a substantial number of the residents are recruited from one employment or industry, though this has its dangers. Mining towns, steel towns, and cotton towns offer too little variety, and are vulnerable to slumps.

Cinemas, theatres, pubs, clubs, dance-halls, and snack-bars all play an important if undefined part in community life, and religious organisations, through their guilds, mothers' unions, and clubs, unite people more strongly than is generally understood. In a new community, activities which link up the new life with the old have special value. Churches and religious organisations, gardening associations, make-and-mend groups, play centres for children, whist-drives, community singing, rabbit clubs, political bodies, sports clubs, and drama clubs are all part of a complex social pattern; and most of them need some focus in a building. Since people like small associations, large and imposing social centres are not necessarily the most attractive. Simple temporary buildings provide a good start: the people themselves can be left to decide on the shape and character of permanent quarters.

Those who plan communities must allow for the divine cussedness of humanity. Local communities are not the only social relationship open to people nowadays—they can stretch feelers far beyond their own towns. Nor do well-organised activities necessarily reflect a good community spirit: they may be the hobby of a small active group. The most that planners can do is to provide easy opportunities for people to meet each other, to overcome shyness, and to learn to take civic responsibility.

1. *Planning*, 1949, vol 15, no. 296. From Political and Economic Planning, 16, Queen Anne's Gate, London, S.W.1.

SUGARS AND BACTERIA

ACID and gas, pink sugar tube and bubble, are traffic lights to the routine bacteriologist, and the product of perhaps a dozen enzyme reactions to the biochemist. The processes whereby animal, plant, or bacterial cells get their energy from carbohydrates are similar, and glucose suffers much the same fate in the boxer's biceps as in a yeast cell. Fermentation reactions are still one of the simplest ways of classifying organisms, and without them the intestinal pathogen in fæces would be as safe as the needle in the haystack. In the laboratory the coloured plugs of sugar tubes indicate a variety of substances from complex polysaccharides (like starch) to hexahydric alcohols (like inositol, which is a growth factor for animals as well as bacteria). For reliable diagnostic tests these substances must be pure, and a useful pamphlet, entitled Sugars and Bacteria, issued by Messrs. Thomas Kerfoot & Co., reminds us to know something of their physical constants.

A SURGEON'S STORY

Mr. R. G. Hogarth's book,[1] while making no pretensions to literary style, is breezy and refreshing. He has a hearty belief in the good things that life has to offer, and his interest in his fellow men has been one of the secrets of his success. His work on behalf of the Nottingham General Hospital and allied institutions must be especially noted; but he has many other interests, including sport in many of its forms.

1. The Trent and I go Wandering By. By R. G. HOGARTH, consulting surgeon, General Hospital, Nottingham. Nottingham: Cooke & Vowles. 1949. Pp. 140. 12s. 6d.

University of Leeds

At recent examinations the following were successful:

M.D.—R. C. Gledhill, J. S. Thorburn.
Ch.M.—R. A. Hall, R. E. Shaw.
Final M.B., Ch.B. (part III).—Nora E. Brown, D. Burrell, Hazel M. Coleridge, R. S. Colwyn, E. L. Copley, Frances M. Cottam, P. H. Daley, W. P. Goodyear, Ida Mather, J. E. Miller, Anne B. Nell, Cynthia M. Perlman, K. Platts, Mary C. Robertson, J. Sagar, M. H. Singer, Doreen W. Steinbrecher, D. J. Stephens, Joyce M. Teasdale, Margaret Winton.

University of Aberdeen

On March 31 the following degrees were conferred:

M.D.—R. G. Simpson (with honours); George Sangster (with commendation); P. H. Beattie.
M.B., Ch.B.—A. R. Adams, Mary P. H. Lewis, Alexander Nicol, N. A. Regan, Joan E. Smith, R. F. F. Steven, J. A. Tallack.

Royal College of Physicians of London

On Tuesday and Thursday, May 3 and 5, at 5 P.M., at the college, Pall Mall East, S.W.1, Dr. N. Hamilton Fairley, F.R.S., is to deliver the Croonian lectures. He is to speak on Malaria with special reference to Experimental, Clinical, and Chemotherapeutic Investigations.

Royal College of Surgeons of England

Dr. Robert I. Harris, associate professor of surgery in the University of Toronto, will be admitted to the honorary fellowship of the college on April 29, when he will deliver a Hunterian lecture on Spondylolisthesis.

Royal College of Surgeons in Ireland

On April 1, J. S. Martin, M. S. Strong, and J. C. de R. Sugars were admitted to the fellowship.

Institute of Child Health

Dr. G. H. Newns has been appointed dean of the Institute of Child Health of the University of London in succession to Dr. W. G. Wyllie, who has resigned.

Digitized by Google

Royal College of Obstetricians and Gynæcologists

A postgraduate course of lectures on obstetrics and gynæcology will be given at the college from Monday, April 25, to Friday, April 29, at noon and 5 P.M. each day. Further particulars may be had from the secretary of the college, 58, Queen Anne Street, London, W.1.

Institute of Laryngology and Otology

On Saturday, May 7, at 11.30 A.M., at the institute, 330, Gray's Inn Road, London, W.C.1, Mr. S. Richard Silverman, PH.D., director of the Central Institute for the Deaf, St. Louis, will speak on the Rehabilitation of the Deaf.

Summer School in Health Education

The Central Council for Health Education will hold its summer school this year at the School of Domestic Economy, Eastbourne, from July 28 to Aug. 11, under the direction of Dr. Robert Sutherland. Further information may be had from the medical adviser and secretary of the council, Tavistock House, Tavistock Square, London, W.C.1.

League of Remembrance

As the League is vacating its present home next month, further materials from hospitals cannot be received for the moment. Negotiations for new premises are in progress and the League hopes to be able soon to resume its help in making up materials and dressings. Communications should still be sent to 48, Bryanston Square, London, W.1.

Princess Tsahai Memorial Hospital

More than half the equipment for this hospital (built in Addis Ababa by British subscriptions) has now been shipped from this country, and other goods will shortly follow. Further purchases, however, are required before the hospital can be opened. Donations to the Princess Tsahai Memorial Hospital Fund should be addressed to the honorary treasurers (Lord Horder and Lord Amulree), c/o Messrs. H. Reynolds & Co., 1, Bloomsbury Court, W.C.1.

Emergency Dental Treatment

The Minister of Health is issuing regulations to simplify the procedure for giving treatment to dental patients who need help urgently, but who do not wish to undergo all the "treatment necessary to secure dental fitness." Dentists have found it difficult to treat these patients quickly, because, to complete form E.C.17, they are required to make a full examination of the patient's mouth. A new form [E.C.17A] which may be used for these casual patients is confined to the following items: not more than two extractions, a general anæsthetic, or a dressing. For each of these items the fee is to be 10*s*.

Blood Transfusion Research Committee

The Medical Research Council have reconstituted this committee which advises them on problems arising in the course of work on dried blood and dried blood products. The following have been appointed members:

A. N. Drury, C.B.E., F.R.S. (chairman); R. J. Drummond, regional blood-transfusion officer, Cardiff; R. A. Kekwick, Lister Institute; J. F. Loutit, director of the M.R.C. radiobiological research unit, Harwell; R. G. Macfarlane, clinical pathologist, Radcliffe Infirmary, and Radcliffe lecturer in hæmatology, Oxford; M. Maizels, clinical pathologist and university reader, University College Hospital; W. d'A. Maycock, M.B.E., superintendent of laboratories, Elstree branch, Lister Institute, and adviser on blood-transfusion to the Ministry of Health; P. L. Mollison, director of the M.R.C. blood-transfusion research unit; R. R. Race, director of the M.R.C. blood-group research unit.

Travelling Fellowships

The Medical Research Council invite applications for the following travelling fellowships for 1949–50:

Rockefeller Medical Fellowships.—These fellowships are intended for graduates resident in this country who have had some training in research and who wish to work at a centre in the United States or elsewhere abroad, before taking up positions for higher teaching or research in the United Kingdom.

Dorothy Temple Cross Research Fellowships in Tuberculosis.—These fellowships are open to British subjects who wish "to devote themselves to the advancement by teaching or research of curative or preventive treatment of tuberculosis." They will, as a rule, be awarded to candidates who wish to study elsewhere than in the United Kingdom.

The fellowships provide a stipend of £650 per annum for a single fellow, and of £900 for a married fellow, together with an allowance for travelling and incidental expenses. Applications should be sent to the secretary of the council, 38, Old Queen Street, London, S.W.1, not later than June 1, 1949.

Association of Independent Hospitals

The independent hospitals, including convalescent homes, epileptic colonies, and other institutions which do not come under the National Health Service, have formed an association to safeguard and develop their interests. Further information may be had from Mr. A. J. Wood, the hon. secretary, National Sanatorium, Benenden, Cranbrook, Kent.

National League of Hospital Friends

Since hospitals were nationalised last July many local voluntary organisations have been set up to maintain personal interest in the hospitals and their patients. These bodies have now formed a National League of Hospital Friends, under the presidency of Lord Luke, to provide them with a centre through which they can exchange information and advice and generally promote their objects. Membership is also open to individuals. A survey made by the British Hospitals Association, which originally sponsored the idea, shows that 175 organisations have been established. Some of these focus round a single hospital, others round a group. In all some 500 hospitals are now covered. The acting hon. secretary of the League is Mr. R. F. Millard, 12, Whitehall, London, S.W.1.

Joint Tuberculosis Council

At its last meeting the council decided to seek an interview with the Ministry of Health on the future status of tuberculosis officers and sanatorium superintendents. The council will also urge that the new Standing Tuberculosis Advisory Committee should contain a representative of the tuberculosis services engaged in field work. The committee is to be asked to consider the whole question of notification of tuberculosis, including the council's published report advocating two separate stages—i.e., (*a*) intimation and (*b*) notification. A set of new standard forms of record for the tuberculosis service was approved and ordered to be distributed to regions, with a proviso that the new forms are of an interim nature and that the council has other proposals under consideration.

Dr. P. W. Edwards was elected chairman of the council in succession to Dr. D. P. Sutherland.

Diary of the Week

APRIL 10 TO 16

Monday, 11th

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Dr. E. R. Cullinan, Mr. Guy Blackburn: Acute Cholecystitis.

Tuesday, 12th

MIDDLESEX COUNTY MEDICAL SOCIETY
2.45 P.M. (West Middlesex Hospital, Isleworth.) Demonstration of cases and specimens.
5 P.M. Mr. D. M. Stern: *Veratrum viride* in the Treatment of Eclampsia. Mr. J. Scholefield: Carcinoma of the Colon.

Births, Marriages, and Deaths

BIRTHS

APPERLY.—On March 26, at Evesham, the wife of Dr. Philip Apperly—a son.
BRUCE.—On March 28, in Edinburgh, the wife of Dr. J. A. Bruce—a daughter.
CURRAN.—On March 26, at Cheam, the wife of Dr. P. J. Curran—a son.
FICKLING.—On March 27, at Northwood, the wife of Mr. B. W. Fickling, F.R.C.S.—a son.
GILLESPIE.—On March 30, at Woking, the wife of Dr. H. H. W. Gillespie—a daughter.
REYNARD.—On March 26, at Drayton St. Leonard, Oxford, the wife of Dr. W. A. B. Reynard—a son.
SCOTT.—On March 29, at Norwich, the wife of Dr. R. H. Scott—a son.
VULLIAMY.—On March 30, the wife of Dr. D. G. Vulliamy—a son.

MARRIAGES

JEFFERSON—GOODWAY.—On March 26, in London, Keith Edmund Jefferson, M.B., to Petronell Goodway.

DEATHS

BROWN.—On March 24, 1949, at Pau, Francis Leonard Brown, M.D. Edin., aged 84.
CAWSTON.—On March 19, at Durban, Natal, S. Africa, Frederick Gordon Cawston, M.A., M.D. Camb.
FAGGE.—On March 26, at Melton Mowbray, Robert Hilton Fagge, M.R.C.S., aged 77.
FRASER.—On March 27, John Henry Pearson Fraser, D.S.O., M.C., B.A., M.B. Camb., aged 76.
NICHOLSON.—On March 11, Gilbert William de Poulton Nicholson, M.D. Camb.

Digitized by Google

STATE LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

WERTHEIM'S OPERATION IN RETROSPECT*

VICTOR BONNEY
M.S., B.Sc. Lond., F.R.C.S., F.R.A.C.S., F.R.C.O.G.
CONSULTING OBSTETRIC AND GYNÆCOLOGICAL SURGEON TO MIDDLESEX HOSPITAL; CONSULTING SURGEON TO THE CHELSEA HOSPITAL FOR WOMEN, LONDON

AT the annual meeting of the British Medical Association, held at Leicester in 1905, Professor Wertheim, of Vienna, read a paper before the gynæcological section in which he introduced and described the operation which now goes by his name (Wertheim 1905).

He claimed as the result of it 40 five-year cures out of every 100 patients operated on, as against the 10 or less obtained by simple abdominal or vaginal total hysterectomy.

So great an advance naturally caused a sensation, and the more so because he asserted that his operation was applicable to just on 50% of all cases of carcinoma of the cervix instead of the 10–15% which were the limit of the lesser procedures.

Abdominal hysterectomy for the disease had been advocated by W. A. Freund as far back as 1878, but the real advance began in 1895, when Ries of Chicago proved by experiments on dogs and on the cadaver that a radical operation on the lines of Halsted's operation for cancer of the breast was perfectly feasible, and in 1896 Clark of Johns Hopkins University first performed it on a living woman. Clark's example was followed by Howard Kelly, while, quite independently in far away Australia, Thring of Sydney was trying the same thing.

Wertheim did not begin his long series till 1898, but to his courage and persistence belongs the credit of establishing the operation as one of the recognised procedures of surgery.

His paper, however, was received with considerable scepticism by the older British gynæcologists of that time, most of whom had not undergone that training in general surgery which renders the mind receptive to and capable of exploiting new ideas; but what chiefly stuck in their throats was the high mortality attached to the operation—30 deaths in the first 100 operations that Wertheim performed, though by the time he read his paper he had reduced the rate to 20%.

It was no use arguing that the only alternative at that time was to operate on 10 out of every 100 patients by one of the lesser operations, cure one or two, and let the rest perish; the minds of the pundits were made up—it was a horrible mortality, and that was that. And this criticism has ever since been a weapon in the hands of the opponents of surgery, though today, with surgeons skilled in it, the operative mortality is very much lower; indeed, my colleagues, Frank Cook and Charles Read have shown that in selected cases it is not more than 3%.

* * *

I was not present at this historic meeting, though I had gone up to Leicester to show certain exhibits at the pathological section; but of course I read Wertheim's paper, and I realised at once the wide vista which it opened. So revolutionary a procedure naturally appealed to the younger and (surgically) better-trained minds; and Cuthbert Lockyer, who was then attached to a small hospital at Plaistow, got Wertheim to go down there and demonstrate his operation, after which Lockyer himself began to perform it, being the first British surgeon to do so. Another of the younger men, Wallace, of Liverpool, by whose premature death surgery lost a great executant, followed suit soon after.

As regards myself, I decided to do the operation so soon as a suitable case came my way; and, since I had only the illustrations in Wertheim's article to guide me, I performed it several times in the post-mortem room at Middlesex Hospital.

In 1906 I opened the abdomen of a patient with advanced disease, only to find the growth irremovable; but early in 1907 I did so again, and that time completed the operation, though the patient died a few days afterwards. Later in the year I tried again, and achieved a successful result.

Comyns Berkeley, with whom at the time I was working in close collaboration, assisted me with all these three operations. At the end of 1907 he performed one himself successfully, with me as his assistant, and for the next seven years we always assisted one another.

In 1908 I joined the honorary staff of Middlesex Hospital, and this promotion greatly extended my field of action, for the hospital had had, for a hundred years, wards devoted to cancer, and in consequence it received a much greater number of cancer patients than any other institution in Great Britain.

RESULTS

By the middle of 1908 Berkeley and I were able to publish an interim report (Berkeley and Bonney 1908) on 18 cases of Wertheim's operation, with 3 deaths. The shortest operation took fifty-five minutes, and the longest two hours. By the end of the year we had performed it 30 times.

In 1913 we reported (Berkeley and Bonney 1913) 71 operations on a three-year cure basis, with an operative mortality of 22% and an operability-rate of 63%. The estimation of our operability-rate was then very easy, for Berkeley and I were the only surgeons performing the operation at Middlesex Hospital and Chelsea Hospital for Women, and all the cases of cancer of the cervix presenting themselves at the outpatient departments came to us.

Later on, as other surgeons began to do the operation and radiological therapy came into the field, it became impossible to disentangle those cases whose treatment was primarily determined by us from those in which it was determined by others, and in all our subsequent publications we assumed that our operability-rate remained at 63% on the good ground that our selection of cases had never varied, being founded simply on whether there appeared to be any chance at all of removing the growth.

Lest anyone think this an exaggerated estimate, I cite my figures for cases of carcinoma of the cervix seen by me in private practice. Between 1910 and 1929 I saw 140 such patients, and of these I operated on 113, an operability-rate of 80%.

* * *

The technique I evolved departed somewhat from that of Wertheim. To begin with, removal of the regional glands was a routine, whereas Wertheim did not touch them unless they were obviously involved. Further, instead of removing only sufficient vagina to form a cap over the cervix, I began by removing half, and later on the whole, of it, and as early as 1908 I had replaced the clumsy vaginal clamps that Wertheim used by the instrument which goes by my name.

Our criterion of operability—a possibility of removal and nothing else—necessarily produced a good many cases in which on opening the abdomen extirpation of the growth was found to be impossible because of gross involvement of the bladder or both ureters. One ureter

* Introductory address delivered at the Conference on Malignant Disease of the Female Pelvic Organs at Newcastle on April 1, 1949.

Digitized by Google

can be successfully resected and reimplanted in the bladder; but if bilateral reimplantation is decided on—and it requires a great deal of consideration—I think today that the colon should be chosen, though I have never done it myself.

In 1916, Berkeley and I published a joint series of 100 cases (Berkeley and Bonney 1916). Our operative mortality was 20%, and 39 of the patients were well five years after their operations. In this paper we classified our cases according to whether the regional glands removed at the operation were or were not carcinomatous, a method I have regularly followed since. Not only is it exact, being found on microscopical examination, but also at that time it served the useful purpose of proving that a proportion of the cases whose glands are involved can be saved by surgery. Some authorities had denied this.

The percentage of gland-involved to gland-free cases in a series is a general indication of the degree of the advancement of growth which the surgeon has tackled, but there is no fixed relation between the involvement of glands and the extent of the cervical growth. Generally speaking, of course, the more advanced the growth the greater the chance of involvement; but carcinomatosis of the glands can co-exist with a very small cervical growth, and conversely the glands are not infrequently found free in cases in which the growth in the cervix is very extensive, and post mortem in persons who have died of the disease.

In 1921 I recorded (Bonney 1921) the first 100 operations performed individually by me, with 20 deaths, 40 survivals for five years, and an absolute operative five-year achievement of 25%. And thereafter I published my personal results only, though Berkeley continued to do the operation as before, and by the time he retired he had performed it between 300 and 400 times. Unfortunately he neglected to keep in close touch with his patients, and lost contact with so many of them that his statistics were of much less value than they ought to have been. As far as they went, however, they showed that his results were substantially the same as mine.

By 1925 (Bonney 1925) I had done the operation 192 times, with results the same as those of four years previously, except that the general mortality had dropped to 16%; and by 1926 (Bonney 1926) I had done 214 operations, with the same outcome but a general mortality-rate of 15·8%.

In 1929, at the Royal Society of Medicine, I reported (Bonney 1929) 265 cases on the five-year basis with 40% cures, and 161 cases on the ten-year basis with 36% cures.

My experience had taught me, what I was the first to enunciate, that 10% of all recurrences occur between the fifth and tenth years (the latest either Berkeley or I have known being the eighth year), and that ten years' survival is 100% cure.

* * *

In that paper I exhaustively examined the comparability of radiological and surgical statistics, and showed that of the various methods of computation not one was impartial, because they contrasted dissimilar groups of cases. Some favoured irradiation and some surgery, but they were all alike in this.

I pointed out that the only accurate comparison was between the results of the pure radiologist and those of the surgeon who operates on a proportion of the cases presented to him and irradiates the remainder. The 100 patients presenting themselves at each man's clinic are substantially similar, and the number of five-year and ten-year cures that each achieves out of *his* 100 cases is the measure of the efficacy of the system of treatment he follows, and as such can be directly compared with the other man's results. And here let me beg radiologists to abandon the division of their cases into stages, for every surgeon who has experience of operating for the disease knows how often the preoperative opinion is found to be quite wrong when the abdomen is opened. These so-called stages introduce into the statistics an element of inaccuracy, and, what is perhaps as bad, make them tiresome and boring. All that matters is the number of patients seen, the number treated, and the number of five-year and ten-year survivals.

In 1930 I delivered a Hunterian lecture at the Royal College of Surgeons, wherein I reported 284 cases on the five-year basis, with an operative mortality of 16·5% and a cure-rate around 40%; and 181 cases on the ten-year basis with a cure-rate around 36%; I also described very fully the technique, dangers, and complications of the operation (Bonney 1930).

There are two methods of assessing the number of cures. In the first method all patients lost sight of or dying of other disease are reckoned as having died of carcinoma, whereas in the second method these cases are excluded from the calculation. I hold that the second method is the right one, but throughout all my communications on the subject I have made a practice of giving both estimates. The difference in the figures resulting from the two methods of computation is considerable when applied to ten-year results; for, as the average age of the patients is over fifty, a proportion of them, in ten years, will surely have died of some disease other than carcinoma, and the number lost sight of will be considerably greater than in a five-year series. The first method of computation, which is Continental in origin, was designed to prevent wilful falsification of results. Those who prefer it, with its obvious errors, must have a very poor opinion of the honesty of their fellow workers.

In 1931 I reported (Bonney 1931) 310 cases, and in 1932 (Bonney 1932) 339 cases with results almost identical with those I have given, and in 1935 the American Gynecological Society honoured me by an invitation to give an address on Wertheim's operation. In it I presented (Bonney 1935) 384 cases on the five-year basis with a cure-rate of 39% or 41%, according to the method of calculation, and 283 cases on the ten-year basis with a cure-rate of 29% or 33%.

In that paper I emphasised the fact that a large number of the so-called stage III cases (styled "inoperable") could be successfully operated on, and I was asked to substantiate my contention by actual demonstration. I was very willing, and so one afternoon at the Women's Hospital, New York, I operated on two stage-III cases chosen by my old friend Gray Ward and his hospital colleagues, and I completed both operations. One of the patients, who had malignant regional glands, died of recurrence some years later, but the other, whose glands were not involved, is alive and well today.

* * *

Finally, in 1941 I published (Bonney 1941) the results of 500 operations on the five-year basis, and 415 operations on the ten-year basis. The paper is so comparatively recent that I will only mention its main conclusions. For the 500 cases the five-year cure-rate was 40% or 43%, according to the method of calculation, and the operative death-rate 14%. For the 415 cases on the ten-year basis the cure-rate was 31% or 36%, according to the manner of computation, and the operative mortality slightly less than 14%.

Of the 500 operations, 300 of the patients were gland-free and 200 gland-involved, and the difference in the results obtained from the two groups was very marked. Thus, of the gland-free group on the five-year basis 53% or 58% were cured; and on the ten-year basis 42% or 49%; while of the gland-involved group only 22% or 23% were cured on the five-year basis and only

Digitized by Google

16% or 18% on the ten-year basis. There was a great difference too in the respective operative mortalities, that of the gland-free group being 10% and that of the gland-involved group 20%. It may be said, therefore, that gland-involvement doubles the risk of operative death, and more than halves the average chance of cure; but, on the other hand, it is to be remembered that all these gland-involved patients, left unoperated on, would have died of carcinoma, for the evidence shows that no method of irradiation at present known cures carcinomatous regional glands.

The absolute operative achievement is the number cured out of every 100 unselected patients seen. Reckoning my operability-rate as 63%, my achievement was 25% or 26% on the five-year basis, and 20% or 21% on the ten-year basis; or, to put it another way, surgery can effect 1 five-year cure out of every 4 unselected patients, and 1 ten-year cure (an absolute cure) out of every 5 unselected patients. This does not exhaust the cures that a surgeon can effect; for, besides the patients he operates on, he has a residuum—larger or smaller as his operability-rate is low or high—from which patients can be salvaged by irradiation.

This paper was my swan-song, so far as the statistics of Wertheim's operation are concerned; for, though I have performed it many times since I reached the 500 mark in 1936, I ceased to keep in routine touch with the subsequent patients, feeling that the addition of 100 cases to the series would shed no new light, and that, after labouring for twenty-nine years to keep in touch with the women I had operated on, I deserved a rest.

* * *

Looking back on the figures I have published at various times, I think one must be struck with their uniformity, for my five-year cure-rate for all cases has hovered monotonously around 40%, and my ten-year cure-rate around 35%. It would be strange if it was otherwise, for over all these years my standard of case selection has never varied and my technique has not changed in material details. The one exception to this uniformity is my operative mortality, which was 20% for my first 100 cases, 14% for the next 200 cases, and 11% for the last 200 cases, and it might be thought that this reduction would be reflected in the cure-rates. But it must be remembered that most of the operative deaths followed operations on patients with very advanced disease, only a few of whom would have figured as cures had they survived.

The figures I have given relate to patients operated on over a span of twenty-nine years, during the larger part of which time none of the accessories, adjuncts, and aids which surgeons now enjoy existed, and the last of them was operated on thirteen years ago. Further, they are the results of pure surgery, for I have not used irradiation either before or after the operations except in a few cases where, the extirpation having been virtually completed, I discovered a mass or nodule so firmly attached to the side wall of the pelvis that its removal was impossible. These patients were treated with X rays; but, despite the fact that the position of the target to be aimed at was accurately known, every one of them died.

There is much evidence of recent years that pre-operative irradiation is helpful, but even at the time when my series was finishing it was not convincing, and to have used it then would have vitiated results obtained by pure surgery. Those that I have obtained are very much the same as those of Wertheim himself, and the other surgeons—including from this country Comyns Berkeley and Fletcher Shaw—who have practised the operation on a large scale and published their results. Those opposed to Wertheim were not backward in hinting that his figures were untrustworthy, but time has proved them entirely honest.

I also have encountered some opposition for keeping the flag of surgery flying, and it has been assumed that I am an opponent of irradiation, which is untrue. What I have done in the past, and what I again do now, is to insist that there are certain cases of cancer of the cervix best treated by surgery, as there are others best treated by irradiation. The views I expressed in my Hunterian lecture in 1930 remain unchanged:

"The truth of the matter probably is that in certain cases surgery, and in others radium, would give the best chance of cure, each case being a law unto itself in this respect, but our investigatory methods are too coarse and imperfect to enable us to discriminate accurately. This is the position at present, but how long it will continue remains to be seen, for the control of the forces of radioactivity is yet in its infancy, and the future may see the power capable of disrupting the very atom into its component parts, harnessed and directed to a degree only dreamed of today. We have, however, to deal with things as they are, not as they may be, and hence I deprecate as altogether premature the appeals which have been made to the younger gynæcological surgeons not to embark on the operative treatment of cancer of the cervix, but instead to take up radium therapy."

Since that was written 19 years ago radioactivity has been the means of greatly increasing our power of destroying life; but alas! not of saving it.

Among the group of cases which should be treated by surgery are those where the growth is refractory to irradiation, and it is of the utmost importance that some method be found by which refractoriness or vulnerability can be distinguished before any treatment is decided on. We must all welcome, therefore, the contribution which Glucksmann and Stanley Way (1948) have made towards an achievement, which, when fully realised, will constitute a major advance in our battle against carcinoma of the cervix.

The specific cure for cancer has not yet arrived—some substance or agent which, put into the body, will single out for death the cancer cell, and/or the factor which energises it, and nothing else. When that day comes, tribute will be paid to Blair Bell, whose work, though it evoked much hostility, largely by reason of his own magnificent egoism, was, I have no doubt of it, along the right path.

Till then, surgery and radiotherapy alike are makeshifts—a humbling thought and one which should discourage the acrimony which has crept into their rival claims.

REFERENCES

Berkeley, C., Bonney, V. (1908) *Brit. med. J.* ii, 961.
— — (1913) *Brit. J. Obstet. Gynæc.* **24**, 145.
— — (1916) *Brit. med. J.* ii, 445.
Bonney, V. (1921) *Ibid*, ii, 1103.
— (1925) *Ibid*, ii, 281.
— (1926) see *Lancet*, ii, 855.
— (1929) *Proc. R. Soc. Med.* **22**, 53.
— (1930) *Lancet*, i, 277.
— (1931) *Aust. N.Z. J. Surg.* **1**, 6.
— (1932) *Brit. med. J.* ii, 914.
— (1935) *Amer. J. Obstet. Gynec.* **30**, 815.
— (1941) *Brit. J. Obstet. Gynæc.* **48**, 421.
Glucksmann, A., Way, S. (1948) *Ibid*, **55**, 574.
Wertheim, A. (1905) *Brit. med. J.* ii, 689.

"... The so-called social sciences encourage students to talk endlessly about alleged social problems. They do not seem to equip students with a single social skill that is usable in ordinary human situations. Sociology is highly developed, but mainly as an exercise in the acquisition of scholarship. Students are taught to write books about each other's books. Of the psychology of normal adaptation, little is said, and, of sociology in the living instance, sociology of the intimate, nothing at all. Indeed, in respect of those social personal studies that are becoming more important year by year, no continuous and direct contact with the social facts is contrived for the student. He learns from books, spending endless hours in libraries; he reconsiders ancient formulæ, uncontrolled by the steady development of experimental skill; the equivalent of the clinic, or indeed of the laboratory, is still to seek."—ELTON MAYO, *Social Problems of an Industrial Civilization*. London, 1949.

Digitized by Google

EXCRETION OF CHLORIDE AND SODIUM AFTER SURGICAL OPERATIONS

A. W. WILKINSON M.B. Edin., F.R.C.S.E.
BARBARA H. BILLING B.A. Camb.
GABRIELLA NAGY B.Sc. Lond.
C. P. STEWART M.Sc. Durh., Ph.D. Edin.

From the Department of Surgery in the University of Edinburgh, and the Clinical Laboratory, Royal Infirmary, Edinburgh

DURING observations made for another purpose it was noted that, for six days immediately after partial gastrectomy, the excretion of chloride in the urine was much reduced below the amount found before operation and at a later period after operation. By combining observations on urinary sodium and chloride excretion with those on nitrogen balance, it has been found that the period of reduced chloride excretion coincides with one of reduced sodium excretion and often with that disturbance of protein metabolism which Cuthbertson (1932) has called the " katabolic phase."

METHODS

From the time of admission, three to seven days before operation, until discharge, ten to twenty-three days after operation, the daily output of chloride in the urine and in gastric aspirations was measured (and expressed according to convention as sodium chloride). The method of Peters and Van Slyke (1932) was used. Sodium was determined by the uranyl zinc acetate method (Butler and Tuthill 1931), and simultaneously a nitrogen balance study was made.

In all, 27 patients and 4 healthy young male controls were studied: 1 patient underwent splanchnicectomy for hypertension, 1 lumbar sympathectomy for causalgia, 19 partial gastrectomy, 5 vagotomy and partial gastrectomy, and 1 gastrojejunostomy. In 20 of these patients an estimate was made of the sodium and chloride content of the food eaten (McCance and Widdowson 1946) and of the intravenous fluid administered in the early postoperative period. The remaining 7 patients were studied in more detail, the intake of salt being carefully measured. All the urine passed in the twenty-four hours from 8 A.M. to 8 A.M. was collected in a 5-litre jar which was suspended from the side of the bed and into which the patient emptied his urinal after use. The stools were collected for each period of twenty-four hours, and fluid aspirated from the stomach before and after operation was analysed.

RESULTS

Classification

For convenience of discussion the subjects are divided into five groups:

(1) Four controls were submitted to various dietary restrictions but not to surgical interference or to anæsthesia.

(2) Nine patients, of whom 5 received the routine postgastrectomy treatment of this unit, and the remaining 4 were submitted to vagotomy (1), gastrojejunostomy (1), lumbar sympathectomy (1), and splanchnicectomy (1). Gastric aspiration was not done in these cases.

(3) Four patients in the immediate postoperative period received intravenous infusions of an enzymic digest of casein ('Casydrol') in amounts which would yield as nearly as possible an intake of 11 g. of nitrogen a day.

(4) Seven patients during the postoperative katabolic phase received, initially by a jejunal tube and later by mouth, a mixture of whole milk, dried skimmed milk, and lactose, the total amount of milk mixture or mixture plus ordinary food being calculated to yield at least 70 g. of protein (11 g. of nitrogen) and 1700 calories a day.

(5) Seven patients were given, as nearly as possible, a constant intake of sodium and chloride throughout the preoperative and postoperative periods, partly by intravenous salt solution and partly by known amounts of salt in the diet.

In all these groups, except the control group, the urinary excretion of chloride after operation was depressed irrespective of the amount of salt given. The time of onset of the depression of urinary chloride excretion varied. Though in some cases a fall in amount began two or three days before operation, which might have been initially related to a reduction in appetite and in food consumption, and in a few the fall was delayed for one or two days after operation, in most cases the fall was abrupt on the day of operation. The depression lasted for five days after operation in 8 patients, for seven days in 7 patients, for eight days in 5 patients, for nine days in 2 patients, and for ten days in 1 patient; in 4 the exact duration was not determined. The total urinary chloride excretion fell below 1 g. a day for two or more consecutive days in 13 patients, and below 2 g. a day in 12 patients. There was no relationship between the time of onset, duration or degree of depression of urinary chloride excretion, and the type of postoperative treatment.

When, after partial gastrectomy, the intravenous intake of sodium chloride was compared with the excretion of chloride in the urine and the loss of chloride by gastric aspiration, it was found that there was retention or accumulation of chloride in the body though only modest quantities of saline (1 litre a day) had been infused. The accumulation of chloride lasted from five to seven days and was later followed by a period when the loss of chloride exceeded the intake.

Group 1—Controls

The two diets for the controls were really designed to clear up some points in relation to the katabolic phase of protein metabolism, and this accounts for their particular form. In each of the diets the nitrogen intake was the same and was based on that of a typical patient after partial gastrectomy. In group A the calorie intake was maintained at or near 2500 calories a day throughout the experiment. In group B the calorie intake was restricted as it usually was after operation, falling to 500 calories a day for the day of operation and the succeeding two days but thereafter rising as in a typical patient. Whereas in group B the salt intake was unrestricted, in group A food was provided which had been cooked without salt and salt was added according to taste, from a weighed daily supply, the unused portion of which was later weighed. During the three days of starvation, in group B salt intake was almost nil, whereas in group A it was maintained at 6–8 g. a day. The daily excretion of chloride varied according to the salt intake; the characteristic patterns which resulted in the two groups are shown in fig. 1. Thus the urinary excretion of chloride in these varieties of food restriction was not related to the protein intake and could be largely controlled by the consumption of salt by mouth. A typical result from a patient after partial gastrectomy on a protein and calorie intake similar to that of the group B controls is shown in fig. 2.

From the work of Benedict (1915) one would expect the urinary chloride excretion to take several days to fall to 1 g. a day or less in fasting people who were well nourished before the experiment began. This is what might have happened in the controls starved of calories and protein if their intake had not been resumed after three days' starvation. In the patients after operation, however, the urinary chloride excretion falls much more rapidly, suggesting that there is some factor causing this which is related to the operation and is additional to the starvation factor.

Group 2—Patients on Routine Ward Treatment

Of 9 patients in this group 5 underwent partial gastrectomy. After operation they were treated by continuous intravenous infusion of saline or glucose solution with

Digitized by Google

two-hourly gastric aspiration for periods up to four days according to individual indications, only small quantities of water or milk and water being given by mouth during this time. Thereafter the intake of food was gradually increased to 70 g. of protein and more than 1800 calories a day, this level being reached by from six to ten days. Of the other 4 patients 1 underwent splanchnicectomy, 1 lumbar sympathectomy, 1 vagotomy, and 1 gastrojejunostomy; in none of these cases was intravenous infusion or gastric aspiration used.

In all cases there was a depression of urinary chloride excretion after operation. This depression occurred in spite of the intravenous administration of more than 10 g. of salt a day in some cases. On the other hand, during the first three days after operation there might be a loss of chloride equivalent to 5–15 g. in the fluid aspirated from the stomach. It seemed curious that, whether or not chloride was lost by suction, the urinary chloride excretion was depressed to about the same degree. The following 3 cases have been chosen as representative of the various features of this group.

Case 1.—A man, aged 36. Diagnosis: hypertension. Operation: left splanchnicectomy. The total daily urinary chloride fell to 1·07 g. on the day of operation; it was 2·72 g. next day, and remained about 1 g. a day for another five days. There was no intravenous infusion or gastric aspiration. The period of increased nitrogen excretion coincided with that of depressed chloride excretion.

Case 2.—A man, aged 52. Diagnosis: chronic duodenal ulcer. Operation: gastrojejunostomy. The urinary chloride excretion was about 5 g. a day before operation; little urine was passed for twenty-four hours after operation, but thereafter the volume was good; chloride excretion only once exceeded 1 g. a day in the next five days, after which the amount rose to above 5 g. a day. No intravenous fluid was given. About 0·5 g. of chloride was removed in the gastric aspirations, which were stopped twenty-four hours after operation.

Case 3.—A man, aged 38 (fig. 2). Diagnosis: chronic duodenal ulcer. Operation: partial gastrectomy. Over 3 g. of chloride appeared in the urine on the day of operation and the next day, but thereafter for five days there was less than 1 g. a day, and for three more days less than 2 g. a day. Gastric aspiration was continued for four days, and large volumes of fluid were withdrawn, containing up to 7 g. of chloride on the last day. Intravenous infusion was continued until the fifth postoperative day, and by this means more chloride was given than was withdrawn by gastric aspiration.

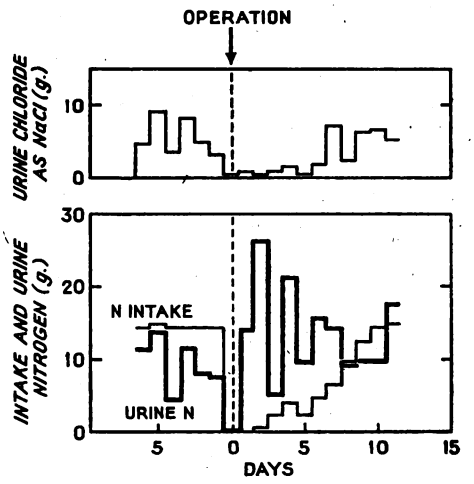


Fig. 2—Urinary chloride excretion and nitrogen intake and output, before and after partial gastrectomy for duodenal ulcer in case 3.

In all the cases the nitrogen balance was also studied. The postoperative increase in nitrogen excretion (which is a more striking and constant phenomenon than the negative nitrogen balance) coincided roughly with the period of decreased urinary chloride excretion. Whether this was a chance occurrence, or whether the two phenomena are related as part of a general metabolic disturbance, these observations were insufficient to decide. Direct proof of this relationship is very difficult, but indirect support might be obtained if it were found that the two phenomena were inseparable under different conditions.

Group 3—Intravenous Administration of Casein Hydrolysate

In this group the nitrogen intake immediately after operation was kept at a moderate level throughout by the intravenous infusion of a casein hydrolysate (casydrol). The casydrol infusion was maintained until food intake was restarted, and because of this the intake of chloride was maintained, being indeed greater in the five or six days after operation than in both the preoperative period and the subsequent postoperative period. In spite of this the excretion of chloride fell to the low levels observed in the cases of group 2, and it returned to about the preoperative level only after the usual period of from five to eight days. Indeed it was particularly striking that the urinary chloride excretion returned to the preoperative level at a time when the chloride intake was lowest because of the transition from intravenous infusion to oral feeding. This may be due in part to the known delay in excretion of salt given intravenously.

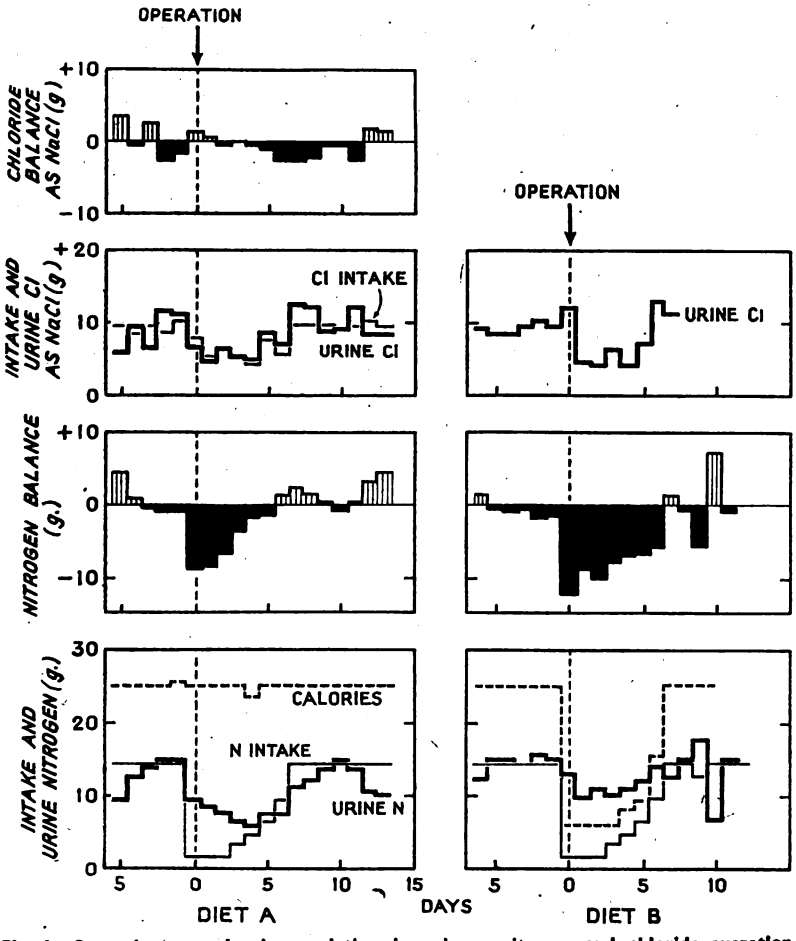


Fig. 1—Control group showing variation in urinary nitrogen and chloride excretion on the two types of diet. In this figure the "operation" is of course imaginary.

Digitized by Google

These features are illustrated in fig. 3. In this patient the salt intake, before operation and when ordinary feeding was resumed after operation, was estimated from tables to be about 7 g. a day. Only on the second postoperative day did the intake derived from intravenous saline or casydrol fall below 7 g. a day; on the other five days the intravenous salt intake was about 10 g. a day. The urinary chloride remained at less than 1 g. a day until the fifth day, when a rise began which was much more rapid than the rate of increase in the oral intake of food and of salt.

In these patients, after operation, there was also a considerable increase in nitrogen excretion, and the period during which this took place again coincided with the period of decreased chloride excretion. During the casydrol infusion there was an abundant intake of protein, but the calorie intake (1000–1100 calories a day) was inadequate. In 2 cases of this group large amounts of chloride were removed in the gastric aspirations, but this made no significant difference to the extent or duration of the phase of lowered chloride excretion. Further, the amounts lost in this way were far less than the amount of salt supplied intravenously as casydrol and as saline; hence in all cases there was a considerable retention of chloride in the first week after operation.

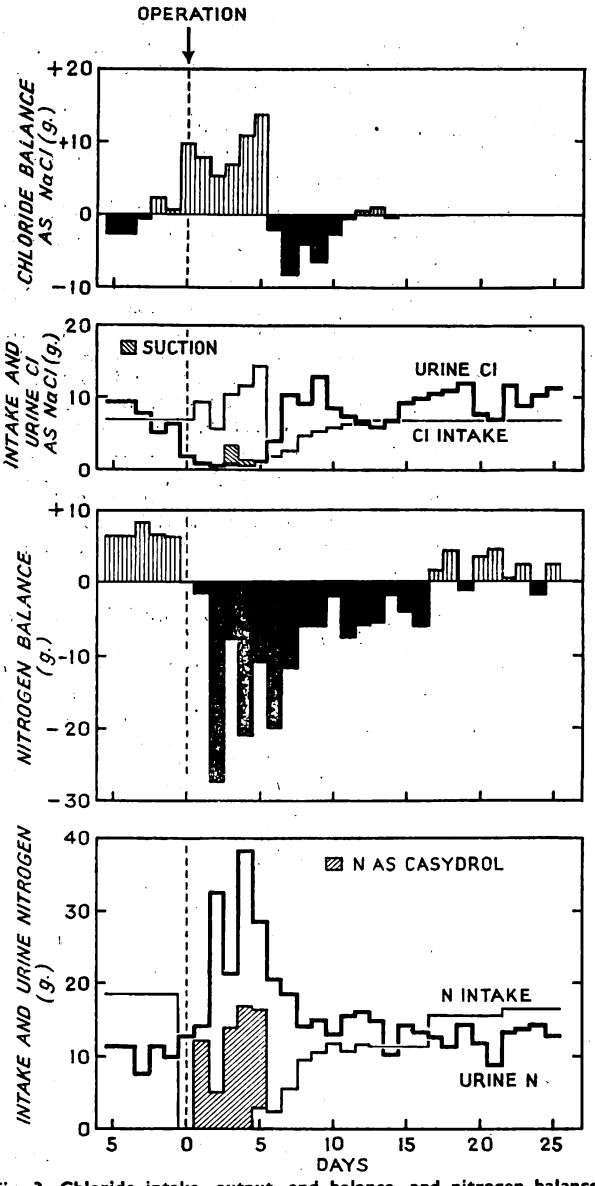


Fig. 3—Chloride intake, output, and balance, and nitrogen balance, intake, and output charts before and after partial gastrectomy for duodenal ulcer in a patient who was given intravenous hydrolysate for five days after operation. Negative nitrogen balance of 12·86 g. has been omitted on day of operation from nitrogen-balance graph.

Group 4—Milk Mixture

In this group there were 7 patients, who during the postoperative katabolic phase received, initially by a double-lumen tube inserted at operation into the distal limb of the jejunum and later by mouth, a mixture of whole milk, dried skimmed milk, and lactose. The total amount of this mixture given daily was calculated to yield 90 g. of protein and 1700 calories a day; on some days this intake was not achieved, on others it was exceeded. The salt intake was never less than 4 g. a day; while the intravenous infusion was being given it was about 10 g. or more a day. In 3 of these patients the urinary chloride excretion was less than 1 g. a day for two or more days, in 3 less than 2 g., and in 1 less than 3 g.

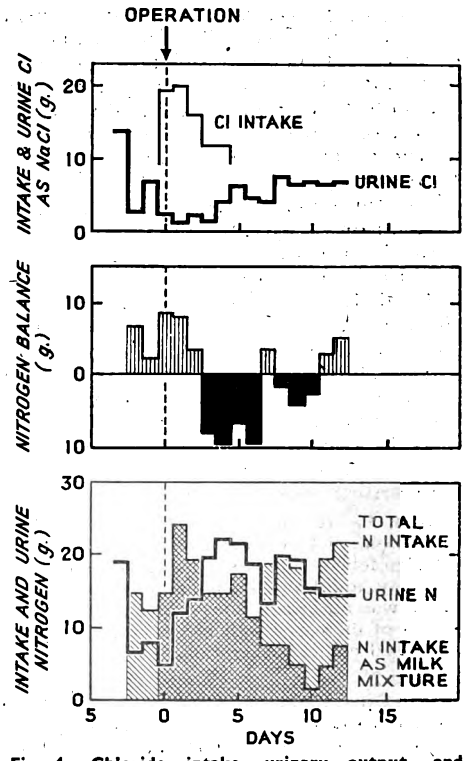


Fig. 4—Chloride intake, urinary output, and balance in case 4, who was given milk mixture after partial gastrectomy.

Case 4.—A man, aged 52 (fig. 4). Diagnosis: chronic duodenal ulcer. Operation: partial gastrectomy. In this case salt was added to the milk mixture so that the daily intake was considerably greater than in most of the patients of this group, reaching nearly 20 g. on the day after operation. In spite of this large intake of salt, urinary chloride excretion remained low for four days after operation. Some of the salt taken in the milk mixture was lost in stools passed on the third, fourth, and sixth days after operation.

The pattern of chloride excretion was similar to that found after operation in the preceding groups. There is no essential difference in the urinary chloride excretion in the patients of group 3, who received a large amount of salt and a high-protein but low-calorie intake immediately after operation, and those in group 4, who received a smaller salt intake but adequate protein and calories. Whether the salt is given by the intravenous route or by mouth also appears to be immaterial.

Group 5—Constant Salt Intake

There remain to be considered 7 patients who were studied in more detail. In addition to nitrogen, sodium, and chloride balances, an attempt was made to keep the salt intake constant throughout the period of study before and after operation. A diet of known composition but low in salt was provided, the food being cooked without the addition of salt. The patient was supplied each day with a weighed quantity of salt which he sprinkled directly on his food according to his taste. During the immediate postoperative period, before this diet was given and after intravenous saline had been discontinued, the requisite amount of salt was given by

Digitized by Google

mouth in the form of saline solution flavoured with orange-juice. An ample supply of distilled water was allowed, and the amount consumed was measured daily. Tea and other beverages were made only with distilled water from this daily allowance. In addition, in the patients of this group, the sodium and chloride contents of the stools were measured.

Five patients each exhibited a reduction in urinary excretion of sodium and chloride in the first seven or eight days after partial gastrectomy. The onset of this reduction was delayed until the second or third day in 2 patients. There was a small reduction in sodium and chloride intake in 4 patients for one, two, or three days, but this was not of the same order as the reduction in daily urinary output. In these patients there was considerable retention of both ions for eight days after operation, but retention of chloride exceeded that of sodium from the third to the seventh day. In 2 patients who were followed for a sufficiently long time, it was found that later this excess was excreted.

In 1 patient of this group potassium, phosphorus, and sulphur balances were also studied, but the results are somewhat equivocal, and further studies are being undertaken before the work is reported in detail.

Case 5.—A man, aged 43 (fig. 5). Diagnosis: chronic duodenal ulcer. Operation: partial gastrectomy. Salt intake was controlled before and after operation. Urinary chloride and sodium excretion were reduced from the day of operation. There was considerable retention of both chloride and sodium for seven days after operation, coinciding with the period of increased urinary nitrogen excretion and of negative nitrogen balance.

In 1 patient after vagotomy there was immediate retention of both sodium and chloride, though urinary chloride excretion was not depressed until more than five days after operation, when it fell below 2 g. a day. There was a reduction in sodium and chloride intake shortly after the fall in urinary chloride excretion; on the other hand, there was retention of both sodium and chloride after operation. In another patient after gastrectomy and vagotomy the sodium chloride intake unfortunately varied widely; nevertheless the urinary sodium and chloride excretion fell after operation in spite of intakes of up to 18 g. of salt a day, and there was a considerable retention of sodium and chloride in the immediate postoperative period.

In all these patients the increased urinary nitrogen excretion coincided with a reduced urinary excretion of sodium and chloride ions during the seven or eight days immediately after operations such as partial gastrectomy. These phenomena were not disturbed by considerable variations in the amounts of the intake of salt, water, protein, or calories, or in the routes by which these have been given.

DISCUSSION

The most obvious explanation for the reduction in urinary chloride excretion after operation would be lack of intake of salt during the usual period of postoperative starvation or reduced food intake. The coincidence of the reduction in urinary chloride excretion with the postoperative increase in urinary nitrogen excretion associated with the katabolic phase appears at first sight to support this explanation. The postoperative protein breakdown occurs, however, in spite of maintaining oral or jejunal protein and calorie intake at levels known to be adequate, and it is now recognised to be independent of the postoperative protein and calorie intake, though postoperative starvation does somewhat increase the severity of the katabolism. Similarly, when salt intake was maintained by intravenous and oral routes, it was found that urinary excretion of chloride was still reduced after

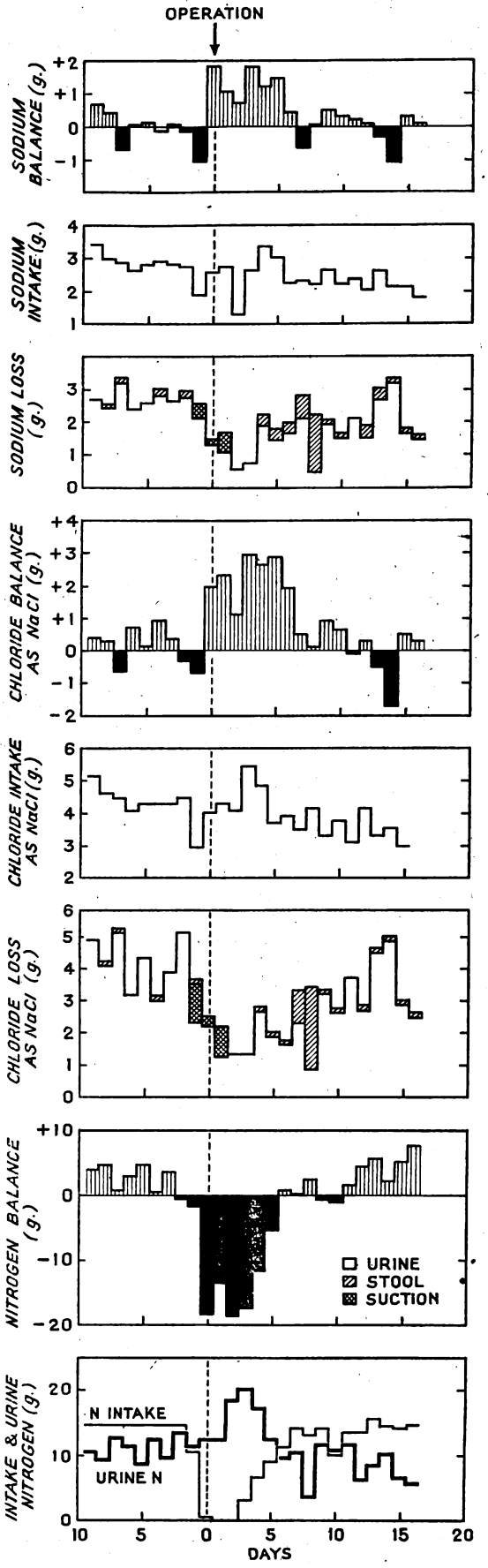


Fig. 5—Sodium, chloride, and nitrogen intake, output, and balance before and after partial gastrectomy for duodenal ulcer in case 5, whose intake of sodium and chloride was controlled.

Digitized by Google

operation. Detailed studies of sodium and chloride intake and output have shown that there is a retention of both these ions during the week immediately following major surgical operations of different types. Others have found similar reduction in urinary chloride excretion after severe accidental injury of various kinds (E. D. Barlow personal communication). We have observed the reduction in chloride excretion also in 2 patients who, probably because of depletion of their protein reserves, did not exhibit an increase in urinary nitrogen excretion after major orthopædic operations.

It is clear that the decrease in chloride excretion during the postoperative period is an expression not merely of a failure of intake but also of some active process leading to a retention of chloride and sodium. The coincidence in time between the retention of inorganic ions and the loss of nitrogen shown in the katabolic phase suggests that the two phenomena may be related.

It has been suggested that the retention of sodium and chlorine is to compensate for the loss of potassium from tissue broken down as part of the nitrogen katabolic phase. If this were the case (though a preliminary study throws some doubt on previous reports of excessive potassium loss), one would expect the sodium retention to be equivalent to the potassium loss.

It seems likely that the retention of sodium with chloride after injury or operation is related to the inflammatory reaction to injury, especially since there is now evidence not only of accumulation of increased quantities of sodium and chloride in damaged tissues after injury but also of mobilisation of sodium and chloride from other, undamaged, tissues (Fox and Baer 1947, Ricca et al. 1945).

In other words, the evidence, incomplete though it is, suggests that the sodium and chloride retention after injury forms a part of a complex response associated with the inflammatory reaction, and that the increased protein breakdown is another part of this response, the two parts both being effects of a common cause rather than one being the cause of the other.

These observations have important practical implications. Current practice is to give saline intravenously during the immediate postoperative period on the ground that there is salt depletion witnessed by depressed urinary chloride excretion. This low chloride excretion, however, seems to be the result of sodium and chloride retention referred to the body as a whole, the distribution of these ions within the body being altered. It is obvious that the whole question of intravenous therapy (particularly of saline therapy) in the immediate postoperative period needs re-examination in the light of these findings. Discussion along these lines must, however, await the results of further experiments designed to extend knowledge of the processes leading to the observed retention of chloride and sodium.

SUMMARY

The observation of a reduction in urinary chloride excretion during the six days immediately after major surgical operations led to further investigation and to the demonstration of a coincidence of reduction in urinary chloride excretion with the increased nitrogen excretion of the katabolic phase.

Detailed observations of chloride excretion were made in 4 healthy controls and 27 male patients after various surgical operations. The significance and possible applications of these investigations are discussed.

We wish to thank Sir James Learmonth for providing clinical facilities and for his continued interest in the work. We are indebted to the four students who volunteered as subjects in control experiments, and to the dietitians who provided the controlled diets. Without the coöperation of the nursing staff these studies would have been impossible, and we wish to emphasise the importance of their help. A grant was made to one of us (C. P. S.) by the Medical Research Council for technical assistance and materials; and one of us (A. W. W.) has held the Syme Surgical Fellowship of this university during the course of these studies.

REFERENCES

Benedict, F. G. (1915) A Study of Prolonged Fasting. Washington; p. 203. Cited by Lusk, G. (1928) The Elements of the Science of Nutrition. 4th ed., London.

Butler, A. M., Tuthill, E. (1931) *J. biol. Chem.* **93**, 171.

Cuthbertson, D. P. (1932) *Quart. J. Med.* **1**, 41.

Fox, C. L. jun., Baer, H. (1947) *Amer. J. Physiol.* **151**, 155.

McCance, R. A., Widdowson, E. M. (1946) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 235, 2nd ed.

Peters, J. P., Van Slyke, D. D. (1932) Quantitative Clinical Chemistry. London; vol. II, p. 833.

Ricca, R. A., Fink, K., Steadman, L. T., Warren, S. L. (1945) *J. clin. Invest.* **24**, 140.

TREATMENT OF A STAMMERER IN THE SECONDARY STAGE OF STAMMERING*

M. C. CRICKMAY

DIRECTOR, SPEECH CLINIC, VICTORIA PUBLIC SCHOOLS, CANADA

THE secondary stage of stammering is the stage when the stammerer has recognised the unpleasant aspect of his speech hesitancies and has therefore begun to fear stammering. This fear causes him to devise tricks whereby he can avoid, postpone, and initiate the speech attempt, and release himself from the block—tricks which quickly become habitual and automatic and are incorporated into the original spasm pattern. Here these bad reaction habits are called secondary symptoms of stammering, and the stammerer who has developed these habits is said to be a secondary stammerer.

The treatment I shall describe is based on the beliefs that (1) a secondary stammerer will never entirely free himself from the fear of certain words and situations, and (2) that a secondary stammerer who has developed habits of avoidance, postponement, and disguise as a reaction to his blocks will never break these habits by merely experiencing a period of free speech. Therefore, instead of working to achieve these periods of free speech by trying to distract the stammerer's attention from his speech, and preventing the occurrence of his blocks, the purpose of this treatment is to draw the stammerer's attention to his speech and train him to modify the form of his speech abnormality. In other words, the stammerer is trained not to avoid his blocks and fears but to work with them and control them. This can be achieved by setting up four goals.

FIRST GOAL

The first is to inculcate the principles of non-avoidance of speech situations and feared words. The secondary stage of stammering is characterised by word and situation fears which range from a slight uncertainty to a state of panic so extreme that the stammerer is incapable of any intelligent effort. Since fear always entails the expectation of unpleasantness, the stammerer wants to avoid that unpleasantness. The avoidance shows itself in many ways, but particularly in the substitution of another word for the feared word, and in the refusal to enter situations in which stammering is likely. It needs to be impressed on the stammerer that we never conquer fear by running away from it, we merely increase it; hence if he allows himself to avoid feared words and situations he will increase his fear of these particular words and situations, and of words and situations closely associated with them. In eliminating the avoidance reactions the stammerer must be trained first to become fully aware of his habits of avoidance by keeping note of situations and words which he did avoid, and secondly to reject these habits by developing a conscience which will penalise the tendency to avoid. It must be impressed

* Read before the International Conference of Speech Therapists, London, September, 1948.

Digitized by Google

on him that non-avoidance of his blocks and fears is a cardinal principle of this therapy, for it is only by learning to control them that he will gain any freedom from them.

SECOND GOAL

The second goal is to train the stammerer to recognise his own particular spasm patterns—i.e., he must know what devices of avoidance, postponement, and release characterise his particular type of stammering; for not until he recognises these devices in his speech will he be able to eliminate them from it. Those unacquainted with the phenomenon of stammering would imagine that a stammerer would know what he does as he gets blocked; but this is not so. Until the matter is consistently brought to his attention, the stammerer seldom has any idea what particular form his spasm pattern takes, even when the block has only just occurred.

The speech therapist must guide the stammerer in the study and analysis of his stammering symptoms—by drawing his attention to them when they occur and describing to him exactly what took place; by imitating them to him, and requiring him to imitate them; by making phonograph recordings of them; by encouraging him to watch himself in a mirror as he blocks; by giving him assignments to collect characteristic samples of his stammering behaviour; and finally by having him write out a detailed symptom analysis of his stammer.

THIRD GOAL

The third goal is to train the stammerer to use the expectancy of stammering in such a way as to change the form of the spasm to one that will have less abnormality and interruption. Experiment has shown that in stammering the preparatory sets determine the form of the stammering block, and are the cause of the stammerer's feeling of compulsion. Van Riper (1937) defines the term "preparatory set" as "a pre-stimulus neuromuscular adjustment which selects, determines, and controls the response to the expected stimulus." In any reaction-time experiment, as Van Riper points out, there are usually (1) a warning signal, which gives rise to (2) a neuromuscular adjustment, consisting of tiny rehearsal movements of appropriate muscle tensions which, when (3) the expected signal occurs, lead immediately and involuntarily to (4) the predetermined response. In any stammering block the above sequence is usually present. The stammerer feels that he has no control over this stammering performance, and that he is compelled to react in this abnormal way. "The reason for this feeling of compulsion lies in the power of the preparatory set to determine and control the response to a signal. The runner with a preparatory set to run at the command will run even though the starter cries 'Jump!'" (Van Riper 1937).

In experiments at the University of Iowa under Dr. Wendell Johnson, and at Western Michigan College of Education under Dr. Van Riper, it proved possible to produce various types of stammering reactions by teaching different preparatory sets, and in 83% of the stammerers with whom this procedure was attempted the experimenter was able to control the reaction by controlling the conscious preparatory set. Moreover, it was found that, as these preparatory sets were assumed time after time on the appearance of a feared word, they tended to become habitual and less conscious, until at length the new reaction often occurred without any voluntary assumption of the new preparatory set. The investigators therefore asked themselves whether it would not be possible to train the stammerer to assume a preparatory set that had little vocal abnormality and interruption to communication. This question can now be answered in the affirmative. Further experiments have shown that it is possible to train him to use the expectancy of stammering as a signal to reject his old spasm pattern and to assume a new preparatory set that has less abnormality and interruption.

The new preparatory set has three dominant features, but in training the stammerer to use this set it is advisable for him to work on only one feature at a time.

1. The speech attempt should be made from a state of articulatory quiescence rather than from a highly tensed musculature. The stammerer must learn that it is possible to make the speech attempt from a state of rest even though he is full of fear and certain he will stammer. To this end he is asked to select a feared word and a feared situation. It is then pointed out to him that in his old spasm pattern he would attempt to say the word from a highly tensed musculature, and he is told what particular area seems to be the most tense—the lips, the tongue, and so on. He is then asked to keep this focus of tension as relaxed as possible at the moment of the speech attempt. His efforts should be limited to reaching this one goal until he has succeeded in making the speech attempt from a state of rest in eight or nine much-feared words and situations. At this stage it is unimportant if he stammers after the speech attempt, but it is important that he start the feared word without preliminary tension, for by doing this he is destroying one of the most dominant features of the old preparatory set.

2. The air flow or voice flow has to be initiated simultaneously with the speech attempt. A secondary stammerer will almost always place his mouth into position for the first sound of a word before starting the vocalisation or air flow. He must be made aware of this preformation, and then trained to replace it by carefully initiating the air or voice flow with the speech attempt; and he must learn to do this under conditions of fear.

3. The speech attempt has to be made as a voluntary-movement sequence. In making a speech attempt on a feared word the stammerer almost always makes two mistakes: first, he sees the word in terms of its first sound alone; and secondly, he assumes a fixed position of the tongue, lips, or jaw, as the case may be, to say just that sound. A stammerer must prepare himself to make the initial or feared sounds of a word as a movement. This entails some training in perception—i.e., he must come to realise that words are made up of a sequence of sounds, and that his difficulty is not so much the making of a feared sound as the transition from that sound to the next. To affect this transition the mouth must be kept in motion, contacts must be light lest the movement be interrupted, and the succeeding sounds must be prepared for in mouth and mind so that the movement may have direction.

It will be apparent that each of the three features described in the new preparatory set is in essence merely a description of a speech attempt as a non-stammerer makes it. We all time the moment of speech attempt with air flow or voice flow; we produce sequential movements rather than static positions when we say a word; we use light contacts and fairly relaxed musculature as we speak. A stammerer also does this on his non-feared words; it is only on his feared words that he does all the wrong things. Therefore training him to use this new preparatory set is merely training him to do consciously what he usually does unconsciously.

It might be objected that if a stammerer had to go through such a rigmarole of preparation on every feared word he might prefer to stammer in his old way. This might be true if it were not for the fact that the new preparatory sets become habituated very quickly if they are taught under emotional conditions, and they lead to greatly improved fluency. After relatively few successful experiences the stammerer finds that, the moment a feared word is perceived, these new sets come into play, and to his own surprise he says the word without any difficulty. Having once experienced this he should be sent into normal speech situations to practise his new skills. When he finds himself stammering in his old way he should not stop, or start over again, but try to bring his symptoms under control by loosening his contacts, by bringing in the air or voice flow, and by

Digitized by Google

starting the movement into the second sound. Finally, after the word is spoken, he should cancel the failure by pausing deliberately and saying the word again with better preparation, and he should make a point of using it in another sentence as soon as possible. Thus every fear or block presents the stammerer with a chance of making some speech progress; and, provided he does not allow himself to block in his old way without doing anything about it, in a surprisingly short time the new preparatory sets replace the old ones as the stammerer's automatic reaction to fear of blocking. As soon as he realises that he can control his blocks without any obvious interruption in his speech he loses his fear of blocking; consequently the number of his blocks decrease and he begins to experience the periods of free speech he so much desires.

FOURTH GOAL

The final goal in this therapy is to help the stammerer to recognise and eliminate the mal-attitudes which he has developed as a result of his speech disability, and help him to adopt a more intelligent attitude towards it. These mal-attitudes of shame and embarrassment associated with the act of stammering are one of the outstanding characteristics of the secondary stammerer. They can be eradicated—at least to the point where they no longer handicap him—first by the use of catharsis (he must be encouraged to talk about his past and present speech experiences), secondly by making him aware of the part these mal-attitudes play in perpetuating and intensifying his handicap, and thirdly by teaching him to adopt a new attitude towards his speech. Instead of pretending that his speech is normal, as every stammerer is apt to do, he must be trained to adopt an attitude of unemotional admission and acceptance of his speech as a problem to be solved. The basic reasonableness of this objective attitude must always be emphasised, and the speech therapist must adopt a similar attitude towards his or her own differences and insecurities.

CONCLUSION

The therapy described here has been evolved during the last 15–20 years. It grew out of the belief that teaching a stammerer methods of avoiding and preventing fear and occurrence of stammering blocks (which was the principle underlying most therapies) was unsatisfactory. It was felt that the effects of suggestion and distraction are temporary, and that self-confidence is affected by too many factors to render it a permanent foundation for fear-free speech. This therapy is based on the belief that, since the stammerer is always likely to have fear, and consequent blocking, on certain words and in certain situations, his best chance of security lies in learning how to modify these blocks so that they occur with the minimum of interruption to communication. It is possible to disrupt and eradicate the stammerer's habitual devices to avoid, minimise, and release himself from his blocks—devices which constitute the greatest part of his abnormality—by training him to use the fear of stammering as a signal to adopt a new preparatory set which can prevent the occurrence of his old secondary symptoms. As soon as he realises that he can control his stammering blocks he loses his fear of stammering, and consequently the duration, severity, and number of his blocks decrease. Thus in this therapy fluency and release from fear are the by-products of *controlled* stammering rather than the results of *avoided* stammering.

REFERENCES

Johnson, W. (1936) *J. Exceptional Child.* **3**, vol. 3, no. 1.
Van Riper, C. (1937) *J. Speech Disorders*, **2**, vol. 2, no. 3.
— (1947) Speech Correction. Principles and Methods. New York, 1947.

FACTORS INFLUENCING THE MAINTENANCE OF ANTITOXIC IMMUNITY

MOLLIE BARR, M.Sc. Lond., A.R.I.C.
A. T. GLENNY, B.Sc. Lond., F.R.S.
From the Biological Division, Wellcome Research Laboratories, Beckenham, Kent

RECENT work suggests that it should be possible, with very few injections, so to immunise children at an early age that no further injection would be necessary to maintain adequate protection against diphtheria for the rest of their lives. We have already shown (Barr and Glenny 1947) that hyperimmunised horses continue the production of antitoxin long after injections have ceased, and after a lapse of time maintain a constant level of antitoxin for 12–18 months, this level usually being about a tenth of the value at the end of immunisation. We also showed that guineapigs receiving only two injections of diphtheria formol toxoid gave the usual secondary response followed by a rapid loss of antitoxin, and that after 2 or 3 months the antitoxic titre rose again slowly in the absence of further injections, increasing up to the 6th month; this rise was termed the "delayed response."

We published curves showing that the response to 1 Lf dose of alum-precipitated toxoid (A.P.T.) repeated after 4 weeks was more than double that to 2 Lf doses of a good quality formol toxoid repeated after 4 weeks, when the comparison was made on values 10 days after the second injection; 6 months after this injection, however, the mean level of antitoxin in the A.P.T. guineapigs was lower than that in the animals which had been given toxoid. These results were obtained from many hundreds of guineapigs, but the mean values were those from a dwindling population owing to some deaths during the 6 months' observation.

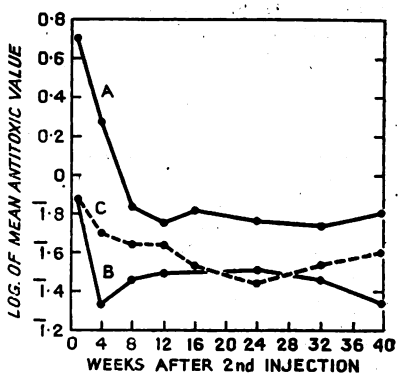
Further work has now been done in following the levels of antitoxin in guineapigs of easily distinguished colours, results being used only from those animals which survived for the duration of the experiment, 10 months.

Three groups of easily distinguishable guineapigs were injected as follows:

Group A received two injections, each of 1 Lf dose of A.P.T. at an interval of 4 weeks.

Group B received two injections, each of 2 Lf doses of toxoid at an interval of 4 weeks.

Group C received two injections, each of 2 Lf doses of the same toxoid at an interval of 6 weeks.



Logs of geometric means of levels of diphtheria antitoxin in guineapigs bled at different times during 40 weeks after second of two injections: A, 1 Lf of A.P.T. at intervals of 4 weeks; B, 2 Lf of toxoid at intervals of 4 weeks; C, 2 Lf of toxoid at intervals of 6 weeks.

Blood samples were taken 10 days, 1 month, 2, 3, 4, 6, 8, and 10 months after the second injection, and the individual sera titrated for antitoxin. The geometric means of the values of animals surviving the 10 months were calculated and are plotted in the accompanying figure.

Curve A (A.P.T.) closely resembles curve 1 (Barr and Glenny 1947), which showed the average results of tests made on many batches of A.P.T. over several years.

Digitized by Google

In our experience the antigenic efficiency of different batches of A.P.T. is remarkably constant, unless minimal doses are used in the test. In curve A the original loss in the first 8 weeks is followed by 8 months with little change: curve 1 showed a slightly smaller loss in the first 8 weeks, followed by a slow fall from 8 to 24 weeks. Curve B does not show so big a delayed response as curve 2 (Barr and Glenny 1947), and this is followed by a fall in value from the 4th to the 10th month, when the mean value was equal to that a month after the injection. Curve C (6 weeks between injections) shows only a gradual loss until the 6th month, after which the curve rises to the 10th month. A comparable experiment was not done in 1947, and this result, showing so pronounced an influence of the interval between injections, needs confirmation.

The antitoxic value in all A.P.T. guineapigs was lower at 8 weeks than at 4, and ten out of eleven values remained lower until after the 32nd week; at 10 months three were the same as at 4 weeks, and eight were lower. Compared with the titre at 8 weeks, five guineapigs at some later time showed a higher titre, but on no occasion was the number with a higher titre greater than the number with a lower titre.

From 12 to 24 weeks none of the nine toxoid animals (group B) had a lower titre, and in at least three the titres were higher than at 4 weeks, and in group C five out of nine had increased in value from the 24th to the 40th week. The percentage amounts of antitoxin present

TABLE I—THE AMOUNT OF DIPHTHERIA ANTITOXIN REMAINING AT DIFFERENT INTERVALS OF TIME AFTER INJECTION, EXPRESSED AS A PERCENTAGE OF THE AMOUNT PRESENT 10 DAYS AFTER INJECTION

Weeks after injection	Group A	Group B	Group C
4	38·6	28·8	77·4
8	13·6	39·4	59·2
12	11·9	42·7	59·2
16	13·7	46·2	46·5
24	11·9	42·7	38·9
32	11·0	39·4	45·0
40	12·8	28·8	54·0

Group A, guineapigs injected twice with A.P.T. at an interval of 4 weeks.
Group B, guineapigs injected twice with toxoid at an interval of 4 weeks.
Group C, guineapigs injected twice with toxoid at an interval of 6 weeks.

at each stage, in terms of the values at 10 days, are recorded in table I, the geometric means being used in calculation. The percentages remaining after 10 months were respectively 12·8%, 28·8%, and 54% for groups A, B, and C. The greatest amount present between 8 and 40 weeks in the A.P.T. group was 13·7%, and the smallest amounts in the toxoid groups 28·8% and 38·9%. It should be noted, however, that group A had apparently reached a fairly permanent level, whereas the values in group B were falling and in group C rising.

Thus two doses of A.P.T. produce far more antitoxin than do two doses of toxoid at the peak of the secondary response, but the rate of loss is much greater after A.P.T. and the delayed response is negligible.

INFLUENCE OF MATERIAL USED IN SECOND INJECTION

Further experiments, in horses, suggest that the nature of the material used for the second injection determines the rate of loss of antitoxin. In one experiment six horses were used which already had some basal immunity as a result of several injections of diphtheria A.P.T. given over 1–2 years. The last injection was given 44 weeks before the start of the experiment. Three of these horses were given 5 ml. of diphtheria toxoid followed 4 months later by 5 ml. of A.P.T.; the remaining three horses received these antigens in the reverse order. The response and rate of loss of antitoxin

TABLE II—RESULTS OF INJECTION INTO 3 BASALLY IMMUNE HORSES OF 5 ML. OF DIPHTHERIA TOXOID FOLLOWED 16 WEEKS LATER BY 5 ML. OF A.P.T., AND INTO 3 HORSES WITH THE ORDER OF ANTIGENS REVERSED

Horse no.	First injection	Level of antitoxin (units per ml.)			Percentage remaining after 16 weeks	Second injection	Level of antitoxin (units per ml.)		Percentage remaining after 16 weeks
		Before injection	At peak	After 16 weeks			At peak	After 16 weeks	
1	Toxoid	2·6	55·0	12·8	23·3	A.P.T.	41·3	16·3	39·5
2	,,	0·65	12·5	4·2	33·6	,,	15·0	4·3	28·7
3	,,	0·60	11·7	4·0	34·2	,,	15·6	4·7	30·1
	Geometric mean		20·0	6·0	29·9		21·3	6·9	32·4
4	A.P.T.	0·33	15·3	0·93	6·1	Toxoid	10·4	6·4	61·6
5	,,	0·75	9·5	1·3	13·7	,,	13·5	5·8	43·0
6	,,	2·0	63·3	9·0	14·2	,,	70·0	17·5	25·0
	Geometric mean		21·0	2·2	10·6		21·4	8·7	40·5

were measured in each case, and the results are given in table II. The responses to toxoid and to A.P.T. were the same, as judged by the geometric mean of the values, which were, however, much scattered. After the first of these injections the loss after 16 weeks was considerably greater in the A.P.T. group, the amount remaining after toxoid being nearly three times that remaining after A.P.T. Slightly more antitoxin remained in the same horses after the second injection of A.P.T. than after the first of toxoid, but nearly four times as much after the second injection of toxoid than after the first injection of A.P.T. The rate of loss after the second injection was less than that after the first, because active production was greater 16 weeks after the last injection, especially in those horses given toxoid, than 44 weeks after the last injection of the earlier treatment.

Further results in support of these findings were obtained in another experiment, in which four horses with basal immunity to both antigens were injected with diphtheria toxoid and tetanus A.P.T. at the same time but at different sites; two other such horses received tetanus toxoid and diphtheria A.P.T. Table III shows the peak response of the horses and the percentage amount of antitoxin remaining 16 weeks after the injections. It will be seen that the loss of tetanus antitoxin was greater than that of diphtheria antitoxin in all the first four horses, there being 2·17–4·23 (average 2·92) times as much diphtheria antitoxin as tetanus

TABLE III—RESULTS OF INJECTION OF DIPHTHERIA TOXOID AND TETANUS A.P.T. OR DIPHTHERIA A.P.T. AND TETANUS TOXOID INTO HORSES WITH BASAL IMMUNITY TO BOTH ANTIGENS

Horse no.	Antigen		Level of antitoxin (units per ml.)				Percentage remaining at 16 weeks		Ratio of remaining diphtheria antitoxin to remaining tetanus antitoxin
			Diphtheria		Tetanus				
	Diphtheria	Tetanus	Before Injection	At peak	Before Injection	At peak	Diph.	Tet.	
7	Toxoid	A.P.T.	3·9	30·0	10·0	65·0	45·0	20·8	2·17
8	,,	,,	1·55	7·5	5·25	65·0	27·6	10·7	2·58
9	,,	,,	1·8	34·7	1·0	40·0	28·8	6·8	4·23
10	,,	,,	0·4	24·0	<0·1	15·0	36·1	13·3	2·71
11	A.P.T.	Toxoid	0·9	5·5	0·2	20·0	30·0	21·3	1·41
12	,,	,,	0·08	8·4	0·2	62·0	10·0	10·5	0·95

Digitized by Google

antitoxin remaining. In the two other horses receiving diphtheria A.P.T. and tetanus toxoid the corresponding figures were much lower—1·41 and 0·95 (average 1·13). It should be noted, however, that these horses had received one more earlier injection of diphtheria than tetanus antigen, to establish basal immunity.

We have found that the levels of antitoxin in horses hyperimmunised against diphtheria or tetanus remain, after an initial fall, constant 2 or 3 years after the last specific stimulus was given, and occasionally antitoxic values increase. Two horses from which 8 litres of blood was taken each week for 26 weeks after injections had ceased increased their level of antitoxin, one by 52% and the other by 67%, during the following 3 months when bleedings had been stopped. There appears, therefore, to be convincing evidence that active production of antitoxin continues long after stimulation has ceased, and it seems probable that such production may continue throughout life if suitable stimulation has been given initially. Any theory of production of antitoxin must therefore explain continued production years after any specific stimulation. Such theories must also explain the speed at which antitoxin is formed after a secondary stimulus. For example, the level of antitoxin in a horse increased by 24 units per ml. from the 6th to the 7th day after an injection of 250 Lf of diphtheria toxoid. The amount of blood in the horse being assumed to be 30 litres, a conservative estimate, the total production was 720,000 units of antitoxin —i.e., for each Lf of toxoid 2880 units of antitoxin was produced in 24 hours, an average of 1 unit every 30 seconds; in 72 hours from the 4th to the 7th day after injection the average rate of increase was 1 unit of antitoxin per minute for every Lf of toxoid injected.

PRODUCTION OF ANTITOXIN

The most generally accepted theory of production of antitoxin is that antibodies are molecules of globulin which in the course of their synthesis have been specially modified by antigen (see Burnet et al. 1941). Cannon (1942), in a review on antibodies and protein reserves, states: "It is difficult to avoid the conclusion that at least some molecules of antigen, by persisting within the antibody-producing cells, can serve later as patterns for the synthesis of fresh antibody-globulin." It is difficult to imagine 20% or more of the antigen remaining intact for several years, during which time continual impressions are made upon the new globulin, or that each molecule of antigen can impress its pattern upon a molecule of globulin once every 30 seconds for 24 hours, or maintain half this rate for 3 days. We therefore suggest that molecules of antigen do not persist as patterns, but that there is multiplication of antitoxin-producing cells or of components within the cells. Either some structure resembling the antigen would be reproduced, or else cells that had built up antitoxic globulin in contact with the original antigen reproduce other cells which then continue to synthesise antitoxic globulin without the need of the original pattern. Pauling's (1940) theory of the folding of a polypeptide chain against the antigen needs considerable modification and expansion. Burnet et al. (1941) have shown that there is a logarithmic phase of antitoxic production and suggested the multiplication of some entity concerned with the production of antibody.

Since McMaster and Hudack (1935) demonstrated the formation of agglutinins by lymph-nodes many other workers have confirmed the rôle of lymphocytes. Ehrich and Harris (1942) worked with agglutinin and hæmolysin, and our colleagues Oakley, Warrack, and Batty (1949) with diphtheria and tetanus toxoids. The theory of reproduction would explain the latent period following a secondary stimulus; if the antigen-bearing antitoxin-producing cells (probably lymphocytes) doubled in number every 8 hours, the possible rate of production of antitoxin would increase five hundred times in 3 days. One other fact which might fit in with this theory of reproduction is that the logarithms of levels of antitoxin reached in some animals after a secondary stimulus lie on a smooth distribution-curve. The experiments recorded here suggest that, when A.P.T. is given, the antigen-bearing cells eventually die off earlier than those bearing plain toxoid.

PLANNING OF LIFELONG IMMUNISATION

The results suggest that it should be possible to lay down a course of immunisation for children that would ensure lifelong immunity. Such a course might consist of two injections of A.P.T. followed at some later date by a boosting dose of toxoid. Once basal immunity has been established, any subsequent injection should not only boost the level of antitoxin but also induce delayed responses to maintain an adequate level. We suggest that at least two injections of A.P.T. should be given to ensure good basal immunity even among those refractory to immunisation.

We hesitate at present to suggest that purified rather than crude toxoid should be used for booster doses to maintain immunity, because doubt is sometimes expressed as to whether diphtheria antitoxin is as efficacious as it was many years ago, before concentration and purification removed most of the euglobulin and some of the associated pseudoglobulin, which would contain any antibacterial substances or other antibodies. Similarly it is possible that purification of toxoid may remove the corresponding antigens which are precipitated by alum from crude toxoid, and thus also included in A.P.T. We suggest that a great deal of work is necessary to determine the conditions under which our work in animals can be transferred to the human field; for instance, only large-scale field experience can justify a departure from the present use of A.P.T., which when carefully prepared and used has given consistently satisfactory results for some years. Improvement is possible and must be continually aimed at, but caution is also needed. Possibly A.P.T. may induce so much antibacterial immunity (assuming this is needed) that subsequent injections are needed only to maintain a certain level of antitoxin; if that is so, purified toxoid or preparations therefrom could be used for subsequent injections. Possibly also Holt's (1947) use of optimal amounts of aluminium phosphate as carrier could be applied to toxoid from which none of the diphtheria bacillary substances have been removed. Only protracted trials can show whether antigens other than specific toxoid and desirable for prophylaxis have been removed in the process of purification.

SUGGESTED RESEARCH

The time is ripe for large-scale investigations, involving coöperation between laboratories, hospitals, and medical officers of health. Students at teaching hospitals could be encouraged to volunteer for a long-term experiment involving bleeding several times during their course. The majority would provide information about the best prophylactic to use as a secondary stimulus for the production of permanent antitoxin, and a minority could be used to work out the optimum interval between the production of basal immunity and subsequent boosting dose. At the same time much work should be done on children, though this would be somewhat limited by the fewer and smaller bleedings. If the work on children were done on a sufficiently large scale and their later history followed, invaluable information would be obtained as to whether the level of antitoxin alone is sufficient to protect against diphtheria.

Digitized by Google

SUMMARY

Production of antitoxin continues for months or years after the last injection of antigen.

It is suggested that cells bearing antigen must multiply, as patterns by which new antitoxic globulin is formed.

It should be possible to devise a course of immunisation for children which would confer lifelong immunity.

Levels of antitoxin in both guineapigs and horses are maintained better if the secondary stimulus is toxoid rather than alum-precipitated toxoid (A.P.T.).

Large-scale experiments on volunteers are needed to test the efficiency of different methods of immunisation. It is suggested that medical students would be useful subjects for observation for five years.

REFERENCES

Barr, M., Glenny, A. T. (1947) *Lancet*, ii, 647.
Burnet, F. M., Freeman, M., Jackson, A. V., Lush, D. (1941) The Production of Antibodies. Melbourne.
Cannon, P. R. (1942) *J. Immunol.* **44**, 107.
Ehrich, W. E., Harris, T. N. (1942) *J. exp. Med.* **76**, 335.
Holt, L. B. (1947) *Lancet*, i, 282.
McMaster, P. D., Hudack, S. S. (1935) *J. exp. Med.* **61**, 783.
Oakley, C. L., Warrack, G. H., Batty, I. (1949) in the press.
Pauling, L. (1940) *J. Amer. chem. Soc.* **62**, 2643.

INTESTINAL RUPTURE FOLLOWING NON-PENETRATING INJURY

GEOFFREY FLAVELL
F.R.C.S., M.R.C.P.
FIRST ASSISTANT, THE LONDON HOSPITAL

Aristotle said: "A slight blow will cause rupture of the intestine without injury to the skin." Since Aristotle's time about 1500 instances of similar injuries have been published: 1313 collected by Counseller and McCormack (1935); 163 by Poer and Woliver (1942); 2 by O'Callaghan (1942); 13 by Kelly (1943); 5 by Bunch (1944); 4 by Hunt and Bowden (1944); 4 by Metheny (1944); and 18 by Ficarra (1944). Of these recorded cases by far the greater number have resulted from comparatively violent causes—traffic accidents, and kicks in the belly during fights, or football. Some were due to ill-judged hernial taxis, and others followed falls, usually of ill or aged people.

The fatality-rate for such injuries was, and is, appalling. Curtis (1887) found 100% mortality in 116 patients. Gage (1902) stated it as 80% and wisely said: "Operate and operate early should be the rule whenever an intestinal rupture is suspected." Counseller and McCormack (1935), reviewing all the available records, calculated the fatality-rate at 73·4%. Poer and Woliver (1942) say it was 61·3% of 163 persons. In the latest series described the rates have been 56% (Ficarra 1944), 50% (Metheny 1944), 33% (Packer 1939), 40% (Bunch 1944), and 69% (Kelly 1943). The explanation of these figures must be sought in the factors which lead to late diagnosis; in the deceptive integrity of the abdominal wall; in the delusive calm, or latent period, which often follows injury; and, in some instances, to the comparative triviality of the blow.

The regions of the bowel most commonly injured are said to be those which are fixed by peritoneum, such as the third part of the duodenum, and the portion near the ligament of Treitz; and those which may most easily be compressed against bony promontories, such as the ileum proximal to the ileocæcal valve where the vertebral column is nearest the anterior wall. But to these anatomical considerations must be added an essential element: the abdomen must be taken by surprise, the blow unexpected, and the muscles relaxed and unguarded.

Zachary Cope (1914) pointed out that after such a blow, when rupture has taken place, a reflex inhibition of peristalsis may last long enough for a plastic exudate of lymph to seal off the rent. After the patient has recovered from the primary shock, or stimulates peristalsis anew by taking food, leakage and consequent peritoneal symptoms will occur. This is the explanation of that "delusive calm" which so often deceives the surgeon and delays intervention.

After such accidents there may be no superficial wound of the abdomen. At first there may be no rigidity, local or general. Leucocytosis and rectal tenderness are late signs—often too late. When much leakage has taken place, gas is often seen below the diaphragm if the patient is radiographed in the erect position; but, on the other hand, such gas may be trapped below the transverse mesocolon in which case radiography is not a safe guide. An abdomen completely silent on auscultation, the presence of "release" pain, or an area of persistent local rigidity which begins to extend justifies immediate laparotomy.

CASE-REPORT

The following history includes all the essential ingredients of one of these injuries, and the patient was under my observation from the moment the blow was struck until his recovery.

A young airman of good physique, began to bat in a unit cricket match at 5 P.M. The third ball of the over did not seem to be particularly fast but broke to leg, glanced up, and struck the batsman just below his umbilicus. He dropped the bat, clasped his belly, and sat down. By the time I reached the crease he was up again and said that he was "just winded for a moment." He was not given out, continued to bat, and made ten runs without mishap. At the end of his innings I saw him again, and this time examined his abdomen. He felt perfectly well but "a bit bruised" where he had been hit. No abrasion or bruise was visible, and there was no local or general rigidity, though he was tender over a point some 2 in. below and to the left of his navel. He left me to have his supper.

At 7 P.M., after a meal of tea and rissoles, he was attacked by burning abdominal pain, reported sick, and was admitted to hospital. On examination he was not shocked and had not vomited. There was local rigidity in the left lower abdominal quadrant, local tenderness, and "release" pain. Peristalsis could be heard on auscultation. I decided however to operate, and opened his abdomen (about three-quarters of an hour later) through a subumbilical paramedian incision. Free fluid was not found, but on the antimesenteric surface of the ileum, some 18 in. from the ileocæcal valve, was a patch of peritoneal soiling round a longitudinal rent ½ in. long. This was repaired with a two-layered Lembert stitch, and the abdomen was closed without drainage. The patient made an uneventful recovery.

COMMENTS

Here are illustrated the apparently trivial but unexpected abdominal blow; the absence of external wounding; the latent period, ended by taking food; and followed by early, but not quite unequivocal, signs of a ruptured bowel. The moral in such event must be that a blow on the abdomen should be watched with no less attention than is a blow on the head; and on reasonable suspicion of perforation the belly should unhesitatingly be explored.

REFERENCES

Bunch, J. R. (1944) *Sth. med. J.* **37**, 717.
Cope, V. Z. (1914) *Proc. R. Soc. Med.* **7**, 86.
Counseller, V. S., McCormack, C. J. (1935) *Ann. Surg.* **102**, 365.
Curtis, B. F. (1887) *Amer. J. med. Sci.* **94**, 321.
Ficarra, B. J. (1944) *Surgery*, **15**, 465.
Gage, H. (1902) *Ann. Surg.* **35**, 331.
Hunt, G. H., Bowden, J. N. (1944) *Arch. Surg.* **49**, 321.
Kelly, E. C. (1943) *Surgery*, **14**, 163.
Metheny, D. (1944) *West. J. Surg.* **52**, 34.
O'Callaghan, D. (1942) *Brit. J. Surg.* **30**, 107.
Packer, B. D. (1939) *Miss. Vall. med. J.* **61**, 218.
Poer, D. H., Woliver, E. (1942) *J. Amer. med. Ass.* **118**, 11.

Digitized by Google

GYNÆCOMASTIA DURING TREATMENT WITH AMPHETAMINE

P. H. TOOLEY
M.D. Lond., M.R.C.P., D.P.M.
PHYSICIAN, DEPARTMENT OF PSYCHOLOGICAL MEDICINE, MAIDA VALE HOSPITAL FOR NERVOUS DISEASES; CHIEF PSYCHIATRIC ASSISTANT, DEPARTMENT OF NEUROLOGY AND PSYCHIATRY, LONDON HOSPITAL

CHRISTOFER LACK
M.A. Camb., M.R.C.S., D.P.M.
PSYCHIATRIC FIRST ASSISTANT, DEPARTMENT OF NEUROLOGY AND PSYCHIATRY, LONDON HOSPITAL

AMPHETAMINE sulphate is now so extensively used that it seems advisable to report the occurrence of gynæcomastia and other apparently œstrogenic effects during therapy with this drug.

Amphetamine sulphate has been recommended for a wide diversity of conditions, including depressive states, fatigue, epilepsy, narcolepsy, certain behaviour disorders of children, dysmenorrhœa, enuresis, migraine, and obesity. The manufacturers of one preparation of amphetamine sulphate report that more than 72,000,000 tablets were supplied to the Services during the 1939–45 war.

Gynæcomastia is defined as excessive size of the male mammary glands. It is usually divided into true and false types. No biopsy was performed in our cases, but the clinical findings pointed to true gynæcomastia—that is, enlargement of the male breast due to hyperplasia of the rudimentary mammary ducts and periductal connective tissue.

After two or three men patients had complained of bilateral slightly tender swelling of their breasts while they were taking amphetamine sulphate, we asked all male patients under treatment with this drug whether they had noted any enlargement of their breasts. A surprising number admitted that they had but said they had not revealed it until directly questioned because it did not seem relevant to the condition for which they were being treated.

ILLUSTRATIVE CASES

Case 1.—A boy, aged 17, who had had enuresis since the age of 9 years, was treated with amphetamine sulphate in view of heavy sleep, though emotional factors appeared responsible for the onset of the symptom. The enuresis completely cleared. There were no signs of overdosage of amphetamine sulphate.

After seven weeks the patient, in response to direct questioning, reported painless swelling of his breasts which had been present for two weeks. There was bilateral firm swelling of the breasts, which were of lumpy consistence, roughly circular, $1\frac{1}{2}$ in. in diameter, and freely movable over the deep tissues but attached at the centre to the nipple. There was no reddening of the skin and no increase in skin temperature, but there was slight tenderness on firm palpation. No secretion appeared when the breast was compressed.

Amphetamine sulphate had been given in a dosage of only 5 mg. every night for five weeks, making a total dosage of 175 mg. up to the time when the breasts enlarged. Amphetamine sulphate has been continued for a further six weeks, and the breast changes have remained the same.

Case 2.—A boy, aged 15, had had persistent enuresis since birth. He showed gross evidence of emotional disturbance, for which there were ample environmental causes. Amphetamine sulphate was given in view of the very heavy sleep. At first the dose was 5 mg. and later 10 mg. every night, and after 21 days, when the patient had had 170 mg., gynæcomastia was noted.

The swelling of the breasts (see figure) was as described in case 1 but considerably larger, and a little fluid, looking like milk, could be expressed from the nipples. The dose was reduced to 5 mg., and the swelling of the breasts diminished but did not disappear. The enuresis cleared.

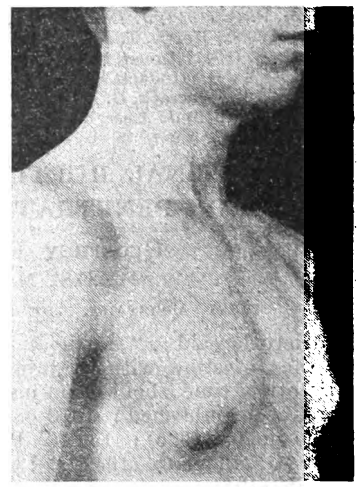
Case 3.—A man, aged 38, an inadequate psychopath with hysterical symptoms, asocial, lacking in energy, and depressed, had previously had myelitis, with residual spasticity of the lower limbs. He was treated with increasing doses of amphetamine sulphate up to 30 mg. a day, and gynæcomastia did not develop until the eighth month of treatment, when he had received 4480 mg.

Amphetamine sulphate was stopped for six weeks, and the breast swelling subsided, only to re-enlarge within three weeks of repeating the amphetamine sulphate in doses of 10 mg. twice a day. The patient gave a history of having had gynæcomastia at the age of 16.

Case 4.—In a man, aged 21, gynæcomastia did not appear until he was receiving a nightly dose of 60 mg. of amphetamine sulphate, which helped his enuresis, produced no signs of overdosage, and did not disturb his sleep.

Case 5.—A psychopathic man, aged 34, who was given amphetamine sulphate symptomatically, developed not only gynæcomastia but also impotence.

In the cases which we have observed the swelling of the breasts has been bilateral, sometimes more pronounced on one side than on the other, and usually slightly tender. The amount of amphetamine sulphate given before the onset of gynæcomastia varied greatly, but it was relatively small in the case of patients near puberty. This would be expected, since boys at puberty may develop gynæcomastia spontaneously, a condition thought to be the result of a temporary imbalance of sex hormones.



Gynæcomastia in a boy aged 15 (Case 2) under treatment with amphetamine sulphate.

A girl aged 9 years, with a severe behaviour disorder of organic origin and symptoms of hyperactivity and distractability, was treated with slowly increasing doses of amphetamine sulphate, leading to considerable improvement of her mental state; but while on a dose of 25 mg. daily, and after she had received a total of 2200 mg. in 98 days, she developed uterine bleeding, which persisted until the amphetamine sulphate was stopped after a month. Since this is so far the only case in our series where such a symptom has developed, it is too early to draw any conclusions, but it is of interest that Karnaky, discussing a paper by Powers (1941), stated that 'Benzedrine' (amphetamine sulphate) might cause uterine bleeding in susceptible patients.

None of our patients developed the symptoms of overdosage which have been described, such as insomnia, restlessness, nausea, dryness of the mouth, or anorexia.

DISCUSSION

Gynæcomastia has been observed in several conditions. Numerous reports have appeared of enlargement of the breasts at puberty, and it is clearly common at that period. Nathanson (1942) found a relative increase in the ratio of urinary œstrogens to 17-ketosteroids in such cases. Gynæcomastia has been reported in association with atrophy of the testes and with testicular neoplasm. In both these conditions adrenal hyperplasia may arise, with a relatively excessive secretion of œstradiol, and it is therefore understandable that gynæcomastia has also been reported with adrenal cortical tumour. Of the pituitary syndromes, it may occur in Cushing's syndrome in the male and, rarely, in acromegaly. It has also been reported in liver atrophy, associated with various infec-

Digitized by Google

tions, and here the cause appears to be the inability of the remaining liver cells to inactivate œstrogen.

Sullivan and Munslow (1942) observed 5 cases without apparent cause in one division of the American army. It would be interesting to know whether by any chance these men were taking amphetamine sulphate.

Gynæcomastia has been noted by Jacobs (1948) in prisoners-of-war in Japanese hands after the arrival of Red Cross parcels after a period of near-starvation. It has also been reported as an occupational disease among those concerned in the manufacture of stilbœstrol.

From these clinical observations it is clear that an increase in the circulating œstrins is the most obvious cause for gynæcomastia. Experimentally, œstradiol stimulates development of the mammary-duct system, and progesterone stimulates development of the mammary alveoli. However, both these substances are without effect in the hypophysectomised animal, and Gomez and Turner (cited by Lewis and Turner 1942) have been led to postulate the release from the pituitary by these ovarian hormones of two secondary hormones, mammogen 1 and 2, which act on breast tissue.

There appears to be little doubt that, in animals, testosterone inhibits mammary tissue, though clinical use of this hormone in gynæcomastia has produced little evidence that in the available doses a similar effect occurs in man. Edwards et al. (1938) and Lawrence (1943) showed that both desoxycortone and adrenal cortical extract can give rise to gynæcomastia.

With these facts at our disposal, and bearing in mind the individual idiosyncrasy of the patient, the local responsiveness of the tissue (which would explain the swelling of one breast more than the other), the loss of libido and impotence, and the occurrence of uterine bleeding, we may speculate about the origin of gynæcomastia in patients treated with amphetamine sulphate.

It is unlikely that amphetamine sulphate has any direct effect, since it bears no chemical similarity to the sex hormones, and it appears to us most probable that it acts at a pituitary hypothalamic level, leading to the increased production of œstrin, probably by the adrenals, and/or a reduction in testosterone, with the result that the œstrin-testosterone ratio is altered. This is at present a purely speculative suggestion, but experimental work is proceeding on both a clinical and a laboratory basis in an effort to throw further light on this interesting problem.

SUMMARY

Cases are described of gynæcomastia developing in patients under treatment with amphetamine sulphate. Other apparently œstrogenic effects are recorded.

ADDENDUM

While awaiting publication this research has continued. (1) Clinical evidence has shown that benzedrine itself is not responsible for the effects described since subsequent batches failed to reproduce symptoms in known cases of susceptibility. (2) Experimentally, with the affected batch hypophysectomised rats reproduced the signs seen in human subjects. The inference is that the effects described were due to an impurity in the amphetamine sulphate of considerable œstrogenic potency. In the course of its preparation amphetamine sulphate passes through a chemical process in which substances closely related in structure to the œstrogens are formed.

Our thanks are due to Dr. Alan Norton, who noted the first of our cases of gynæcomastia, and to Dr. Henry Wilson, under whose care these patients were.

REFERENCES

Edwards, R. A., Shimkin, M. B., Shaver, J. S. (1938) *J. Amer. med. Ass.* **111**, 412.
Jacobs, E. C. (1948) *Ann. intern. Med.* **28**, 792.
Lawrence, R. D. (1943) *Brit. med. J.* i, 12.
Lewis, A. A., Turner, C. W. (1942) *Endocrinology*, **30**, 985.
Nathanson, I. T. (1942) *J. clin. Endocrinol.* **2**, 311.
Powers, E. G. (1941) *Tex. St. J. Med.* **37**, 369.
Sullivan, J. M., Munslow, R. A. (1942) *J. Amer. med. Ass.* **118**, 1443.

FIBROCYSTIC DISEASE OF THE PANCREAS IN AN INFANT

G. G. JONES
M.R.C.S., D.C.H.
MEDICAL OFFICER, LEWISHAM HOSPITAL

ATTENTION was first drawn to fibrocystic disease of the pancreas by Andersen (1938) and Harper (1938). A summary of the three main clinical types (based on Andersen's work) has been given by MacGregor and Rhaney (1948). Briefly they are (1) meconium ileus in the first week of life, (2) marasmus associated with respiratory infection in the first six months of life, and (3) a syndrome clinically indistinguishable from cœliac disease after the age of six months. In the second type the stools usually appear normal though they are offensive and there is an increase in fæcal excretion of fat. In the second and third types there is a tendency to respiratory lesions, commonly as a result of infection with *Staph. aureus*; but, since the cases in which symptoms do not become apparent until after the sixth month of life are usually milder examples of the disease, the respiratory symptoms are less prominent, or, rarely, the infant may escape this complication altogether. The absence of trypsin in the duodenal juice confirms the diagnosis.

CASE-REPORT

The following case shows atypical features. Unfortunately the diagnosis was not considered until the infant was too weak for duodenal intubation.

A male full-term infant born at home on Oct. 4, 1947, weighing 6 lb. Pregnancy was uneventful and delivery normal. The infant was breast-fed. He was admitted to hospital on Dec. 22, 1947 (aged 11 weeks), with a history of slow gain in weight, frequent loose green stools since birth, and an increasing pallor from the seventh week of life. A few days after birth the infant developed a few septic spots in the right axilla which cleared in about two weeks. There had been a slight cough intermittently since birth.

Family History.—The patient had a healthy sister living, aged 9 years. In 1944 there had been a stillborn eight-months fœtus. In both these pregnancies the mother had been admitted to hospital with toxæmia of pregnancy. The mother gave no history of any other serious illness and, on admission to hospital with the infant, was found to be healthy apart from hypochromic anæmia (Hb 60% Haldane), which responded to iron. Her blood Wassermann reaction and Kahn test were negative; she had an adequate yield of breast-milk.

On admission the infant was pale, hypotonic, and lethargic and weighed 7 lb. 13 oz. There was a small healed scar in the right axilla. Throat, ears, and chest showed no abnormality. The abdomen was not distended, and the liver and spleen were not palpable. The stools were frequent (6–8 in twenty-four hours) and semi-formed, with mucus present in small quantities, but were yellow and inoffensive. Radiography of the chest showed no abnormality, and of the long bones no osteoporosis. A blood-count showed 3,500,000 red cells and 15,000 white cells per c.mm. and Hb 48%. There was no Rh incompatibility between the infant's and the mother's bloods. The urine showed no abnormality on admission or on subsequent occasions.

Treatment and Progress.—The infant on admission was treated with iron and ammonium citrate gr. 5 t.d.s., 'Adexolin' 1 ml. daily, and ascorbic acid 50 mg. t.d.s. There was little change in the clinical condition until Jan. 5, 1948 (age 13 weeks), when a scaly desquamating rash developed over the buttocks, trunk, and legs, and pitting œdema of hands and feet. Blood examination showed Hb 36%, red cells 1,910,000 per c.mm., and white cells 8500 per c.mm. (polymorphs 28%, lymphocytes 69%), serum-urea 36 mg. per 100 ml., and total serum-proteins about 3 g. per 100 ml. (insufficient blood was obtained for differential estimation). In view of these findings the infant was given complementary feeds of 'Casydrol' and daily injections of crude liver extract. Bone-marrow biopsy was not done.

Digitized by Google

By Jan. 12 the œdema had spread to the trunk and face, and the abdomen became distended with ascites. On Jan. 25 (age 16 weeks) the infant became pyrexial and developed a persistent cough and signs of consolidation of the left lung base. Within a day or two a left basal purulent effusion appeared, from which penicillin-sensitive *Staph. aureus* was cultured. Blood examination on Jan. 26 showed Hb 42%, white cells 21,000 per c.mm., serum-albumin 2·4 g. per 100 ml., serum-globulin 1·7 g. per 100 ml., and total protein 4·1 g. per 100 ml. The pleural effusion was aspirated on alternate days and penicillin 20,000 units substituted. Intramuscular penicillin was also given. A transfusion of 120 ml. of fresh blood was given on Jan. 27, and after this it was noted that the liver was palpable 2 in. below the costal margin. At this time the infant was being fed on expressed breast-milk, with complementary feeds of 'Prolac,' since the casydrol feeds were not taken well. From the development of the pleural effusion the infant's condition deteriorated. His cough interfered with feeding, and in spite of the persistent œdema his weight fell to 6 lb. by Feb. 1. The fæces on Feb. 8 were light-brown, pasty, and offensive. A wet-film showed no undigested muscle-fibres, no starch granules, but excessive fat-globules were present; total fats 36·9% of dry weight (split 31·9%, unsplit 5%). This estimation was unsatisfactory because it was made on a single specimen. In spite of temporary improvement after further transfusions of fresh blood the infant died on Jan. 21 at the age of 20 weeks after an attack of gastro-enteritis.

Necropsy Findings.—A thin male infant with œdema of dorsa of feet and hands, and of legs; distended abdomen; pale skin; and no jaundice. The abdominal and pleural cavities contained an excess of clear yellow fluid. The larynx, trachea, and main bronchi contained a little creamy pus. The left pleural cavity had a few very fine hair-like adhesions over left lower lobe but no trace of empyema. The right pleural cavity appeared normal. The left lung on section showed saccular and fusiform bronchiectasis of the left lower lobe bronchi with accompanying bronchopneumonic consolidation. The dilated bronchi contained yellow creamy pus. A swab taken from this pus yielded a good growth of *Staph. aureus* which was not penicillin-sensitive. The right lung appeared normal on section. The stomach and intestines had a thin wall, and had the dull opaque appearance often seen in gastro-enteritis in infants. The liver was slightly enlarged; its parenchyma showed fatty infiltration, with areas of diffuse congestion. The gall-bladder and bile-ducts appeared normal. The spleen was slightly enlarged, with firm and congested pulp. The pancreas appeared normal macroscopically. All other organs appeared normal.

Histology.—The bronchi were dilated (bronchiectatic), with desquamated epithelium, and their lumina contained pus cells. The adjacent lung tissue was collapsed, and small abscesses were present in the lung tissue. The liver showed extreme fatty infiltration throughout all lobes, practically no healthy liver cells being left. The pancreas showed a diffuse fibrosis, with young fibrous tissue largely taking the place of the gland parenchyma. Small groups of damaged acini were isolated from one another and surrounded by fairly dense whorls of collagen fibres. Many of the acini were entirely destroyed, and there was a diffuse infiltration with lymphocytes and plasma cells. Many of the surviving acini showed dilated lumina and a tendency for the gland epithelium to assume a low columnar form where this dilatation had taken place. There were also large cystic structures lined with cuboidal epithelium, some of which contained papilliform projections of epithelial cells of no clear pattern. The nature of these cystic spaces was not obvious. They may well have been dilated ducts, but small ones suggested an origin from gland acini. Some of them contained a mucinoid basophilic substance. Occasional groups of much disorganised cells appeared to be surviving islets of Langerhans; they were very infrequent. The kidneys showed no striking lesions.

DISCUSSION

The interesting feature of this case is the development of generalised œdema associated with severe hypoproteinæmia. A slight reduction of the serum-proteins has been occasionally recorded—e.g., by Menten and Middleton (1944)—but I have been unable to find any reports of cases in which hypoproteinæmia was associated with œdema. Anæmia is a not uncommon complication of fibrocystic disease of the pancreas, but it is not usually so marked as in the present case, where it can presumably be explained on the basis of iron deficiency together with the protein deficiency.

It is presumed that in this case the œdema was mainly secondary to the hypoproteinæmia, though other factors, such as anæmia and, in the later stages, cardiac failure, may have played a part in its production.

One point, which has been noted by other workers, is the frequency of a normal macroscopical appearance of the pancreas, even when, as in the present case, there is very little normal tissue to be seen histologically. This is probably the reason why fibrocystic disease of the pancreas (which is not very uncommon) has been clearly recognised only within the last ten years.

There is little doubt that some cases of infantile marasmus which have been attributed to intolerance of protein or fat or to respiratory lesions have been cases of fibrocystic disease of the pancreas. It is therefore important to bear this disease in mind whenever infants do not gain sufficient weight on an adequate food intake, and to examine the pancreas histologically in all infants coming to necropsy with a doubtful diagnosis.

SUMMARY

A case of fibrocystic disease of the pancreas in an infant is described.

An unusual feature of the case was the development of generalised œdema associated with severe hypoproteinæmia.

The pancreas at necropsy in such cases often appears normal macroscopically.

Fibrocystic disease of the pancreas should be considered in any obscure case of wasting in infancy.

I wish to thank Dr. M. O. Skelton for the necropsy report and Dr. E. N. Allott for his helpful criticism in the preparation of this paper.

REFERENCES

Andersen, D. H. (1938) *Amer. J. Dis. Child.* **56**, 344.
Harper, M. H. (1938) *Arch. Dis. Childh.* **13**, 45.
MacGregor, A. R., Rhaney, K. (1948) *Ibid*, **23**, 56.
Menten, M. L., Middleton, T. O. (1944) *Amer. J. Dis. Child.* **67**, 355.

ESTIMATION OF ERGOTHIONEINE IN URINE BY PAPER PARTITION CHROMATOGRAPHY

ELIZABETH WORK
B.A. Camb., Ph.D. Lond.

From the Department of Chemical Pathology, University College Hospital Medical School, London

THE suggested antithyroid activity of ergothioneine (Lawson and Rimington 1947a and b, Astwood and Stanley 1947) makes it important to estimate ergothioneine in biological fluids. The method of estimation described here was developed for the clinical trial of ergothioneine reported by Lawson and Rimington (1947b). Though only roughly quantitative, it seems to be the only reliable one for routine examination of urine.

Methods of Hunter (1928) and Sullivan and Hess (1933) have been tried unsuccessfully in this department for the determination of ergothioneine in urine and in blood. These methods depend on colorimetric measurements; they break down in the case of urine because they do not separate ergothioneine from all the other substances in urine which give similar colours with the reagents used. This separation can be achieved by partition chromatography in which two immiscible solvents are used to separate a mixture of compounds in solution.

PAPER CHROMATOGRAPHY

Paper chromatography has been described for amino-acids by Consden et al. (1944) and applied by Dent (1946, 1947) to biological fluids.

Digitized by Google

TABLE I—R_F VALUES OF ERGOTHIONEINE AND OTHER POSSIBLE CONSTITUENTS OF URINE

Substance	Colour reaction	R_F values	
		Phenol	Collidine-lutidine
Ergothioneine	Pauly Folin-Marenzi	0·88	0·28
Uric acid*	Folin-Marenzi	0·24	0·38
Thiolhistidine	Pauly Folin-Marenzi	0·25	0·57
Sodium uricanate in saline	Pauly Folin-Marenzi	0·36, 0·48	0·79
Ascorbic acid	Folin-Marenzi	0·38	0·42
Glutathione†	Folin-Marenzi	0·12	0·12
Guanine	Pauly	0·27	0·53
Histidine	Pauly	0·77	0·24
Tyrosine	Pauly	0·63	0·53

* In concentrated urine, R_F value in phenol 0·42.
† Cited from Dent (1948).

A drop of the solution under investigation is placed on a strip of filter paper near one end, which is dipped into a water-saturated organic solvent, such as phenol. The second solvent is provided by the water always bound in the pores of the filter paper. The organic solvent creeps past this water phase, carrying along at different rates dissolved substances which distribute themselves along the paper as bands located according to their partition coefficients in phenol and water. After a suitable time the filter paper is dried, and the positions of the substances under investigation are determined by any suitable method, usually a colour reaction.

The positions of the bands are defined by their R_F values—i.e., the ratio of the distance run by the substance to the distance run by the solvent from the application line (Consden et al. 1944). By careful choice of solvent and conditions it is usually possible to separate any two or more substances occurring together.

The method can be made roughly quantitative. The size or colour strength of the spot obtained from a given volume of the solution under investigation can be compared with that produced by a known amount of the substance. Alternatively, the least detectable amount of the pure substance can be determined, and the least volume of test solution necessary to give a detectable band can be assumed to contain this amount. The latter method was used in the work described here.

TECHNIQUE

The technique and apparatus used were those described by Dent (1946).

Single dimensional chromatograms were used to distinguish ergothioneine from other substances in the urines. Ergothioneine was identified on the paper by spraying first with 10% sodium hydroxide and then with phosphotungstic-acid uric-acid reagent (Folin and Marenzi 1929). The position of any blue bands thus produced was marked immediately, for the colour faded in a few minutes and, in the case of urine, a general blue background appeared slowly. Ergothioneine could also be located by the bright red which it produced with diazotised sulphanilic acid in the form of the Pauly reagent (Pauly 1904) after preliminary spraying with 10% sodium hydroxide. In this case best results were obtained after removal of the chromatographic solvent by successive washing with acetone and ether.

It was necessary to concentrate urine before application to the paper, for no ergothioneine could be detected in 50 µl. of urine as passed. So 20 ml. of urine was concentrated almost to dryness in a freeze-drying apparatus, the concentrate was washed into a graduated cylinder with 2 ml. of water, and the volume was made up to 4 ml. with ethyl alcohol. The precipitate, consisting probably of salts and uric acid, was removed by centrifugation, and a suitable volume of the mother liquor was used for ergothioneine estimation.

The ergothioneine used for the control experiments was the crystalline hydrochloride described by Lawson and Rimington (1947b).

RESULTS

Ergothioneine (10 µg.) gave a well-marked band when run in phenol or in a collidine-lutidine mixture. The R_F values of the bands are given in table I, which also shows R_F values of other substances which are likely to occur in urine and which give colours with Pauly's or Folin-Marenzi reagents.

Run in phenol ergothioneine has an R_F of 0·88. All the other substances reacting with the Folin-Marenzi reagent are well separated from it, having R_F values of less than 0·5. Histidine cannot be separated with certainty from ergothioneine in phenol, but since it gives no colour with the Folin-Marenzi reagent it will not interfere with ergothioneine provided Folin-Marenzi reagent, and not the Pauly reagent, is used to develop the bands.

Collidine-lutidine mixture is not as suitable as phenol for separating ergothioneine, since several other substances reacting with the Folin-Marenzi and Pauly reagents have R_F values fairly close to that of ergothioneine.

The choice for routine determinations obviously lay with phenol-water as a solvent, and Folin-Marenzi reagent as an indicator.

50 µl. of normal unconcentrated urine, run in phenol and developed with Folin-Marenzi reagent, gave one band only, R_F 0·24, which corresponds to uric acid, whereas 20 µl. of five times concentrated urine gave two bands at R_F 0·42 and 0·8.

The faster running band was identified as ergothioneine since it gave the characteristic colour reactions, and addition of ergothioneine to the urine increased the strength of the band but did not change its R_F value. The slower band was identified as uric acid, both by addition of uric acid to the urine and by the characteristic yellow it gave when sprayed successively with 0·125 *N* sodium carbonate and a 0·4% alcoholic solution of 2:6-dichloro-quinone-chloroimide (Fearon 1946). The shift in the uric-acid band from R_F 0·24 to R_F 0·42, which was found in chromatograms of concentrated urines, is believed to be due to the effect of the greatly increased amounts of inorganic salts present. The salts move to a large area around the region of R_F 0·2 (Dent 1946) and seem to take precedence there, with the result that the uric acid is forced to its new position at R_F 0·42.

TABLE II—ERGOTHIONEINE CONTENT OF URINES IN TWO CASES OF THYROTOXICOSIS BEFORE AND AFTER TREATMENT WITH ERGOTHIONEINE

Time	Smallest volume of 5 times concentrated urine required to give band (µl.)	Ergothioneine concentration (mg. per 100 ml.)	Total daily excretion (mg.)
Case 1 (male, aged 16):			
Pre-dosage	40	3·8	39
6½ hr. post-dosage	40	3·8	
16 " " "	40	3·8	50
22 " " "	40	3·8	
23½ " " "	30	5·0	
2nd day of dosage	30	5·0	118
3rd " "	30	5·0	85
4th " "	30	5·0	109
5th " "	30	5·0	107
6th " "	30	5·0	115
7th " "	30	5·0	111
8th " "	20	7·5	118
9th " "	20	7·5	152
10th " "	20	7·5	122
11th " "	20	7·5	191
13th " "	15	10·0	183
15th " "	30	7·5	147
Case 2 (female, aged 65):			
Pre-dosage	10	15·0	190
"	10	15·0	178
1st " day of dosage	Separate samples analysed giving total		188
2nd " "	15	10·0	167
3rd " "	15	10·0	152
4th " "	30	5·0	115
5th " "	15	10·0	178
6th " "	15	10·0	180
9th " "	10	15·0	180
10th " "	15	10·0	150
11th " "	10	15·0	206
12th " "	15	10·0	181

Digitized by Google

To determine the least amount of ergothioneine which could be detected by this method, the following amounts of a solution containing 1 mg. per ml. were run in phenol: 5, 7·5, 10, and 15 µl. Positive ergothioneine bands were consistently obtained with 7·5 µl. (containing 7·5 µg.) but not with 5 µl. Therefore the least detectable amount of ergothioneine was taken as 7·5 µg.

Normal urines, five times concentrated, put on at 5, 10, 15, and 20 µl. levels, gave no ergothioneine band at 5 µl., but in 6 out of 8 urines 10 µl. gave a detectable band. This corresponds to a level of 15 mg. of ergothioneine per 100 ml. of fresh urine, or a daily excretion of about 225 mg. The remaining two normal urines gave bands at 15 µl. levels and therefore contained 10 mg. per 100 ml. of fresh urine. The method was checked by adding known amounts of ergothioneine to concentrated urine. The minimum amount of urine giving the ergothioneine band was in all cases lowered by the expected amount.

Ergothioneine excretion was followed in the two thyrotoxic patients on whom therapeutic trials of ergothioneine were being carried out (Lawson and Rimington 1947b). Both patients were given, intramuscularly, a daily amount of ergothioneine hydrochloride equivalent to 79 mg. of free base. For the first 24 hours individual samples of urine were examined; thereafter 24-hour specimens were taken.

The results, shown in table II, are tabulated to show the minimum of concentrated urine required to give a detectable ergothioneine band; also the calculated ergothioneine concentration of each sample and total daily excretion. The two patients responded differently: case 1, with a low initial excretion of 30 mg. daily, showed a rise in rate of excretion within 24 hours of dosage, and the total excretion rose to well over 100 mg. daily. Case 2, with a normal ergothioneine level, showed no change in ergothioneine excretion. In both cases the volume of urine increased considerably after dosage.

DISCUSSION

This method of estimation is at best only roughly quantitative (±50%) and as applied here is only comparative. The minimum levels in urine giving a positive ergothioneine band could be compared by adopting a standard technique. The method was developed at short notice to follow the excretion of ergothioneine during clinical trials, since no other method was satisfactory. The numbers of urine samples which could be applied to the paper to test for minimal levels were limited by time and space; hence quantities of only 5, 10, 15, 20, 30, and 40 µl. were used, which makes the error considerable. The error could be reduced by decreasing the size of the steps and by determining with greater accuracy the smallest detectable amount of ergothioneine. So far as the present figures go, the level of ergothioneine in normal urine lies between 130 and 300 mg. per litre. Sullivan and Hess (1933) estimate the amount of "ergothioneine-like" material to be about 90 mg. per litre of normal urine.

My thanks are due to Mr. R. Denman for technical assistance and to Prof. C. Rimington and Dr. A. Lawson for encouragement and advice.

REFERENCES

Astwood, E. B., Stanley, M. M. (1947) *Lancet*, ii, 905.
Consden, R., Gordon, A. H., Martin, A. J. P. (1944) *Biochem. J.* **38**, 224.
Dent, C. E. (1946) *Lancet*, ii, 637.
— (1947) *Biochem. J.* **41**, 240.
— (1948) *Ibid*, **43**, 169.
Fearon, W. R. (1946) An Introduction to Biochemistry. 3rd ed., London.
Folin, O., Marenzi, A. D. (1929) *J. biol. Chem.* **83**, 103.
Hunter, G. (1928) *Biochem. J.* **22**, 4.
Lawson, A., Rimington, C. (1947a) *Lancet*, i, 586.
— — (1947b) *Ibid*, ii, 906.
Pauly, H. (1904) *Hoppe-Seyl. Z.* **42**, 508.
Sullivan, M. X., Hess, W. C. (1933) *J. biol. Chem.* **102**, 67.

Medical Societies

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

THE annual congress of this society was held in London from March 31 to April 2 under the presidency of Mr. FRANK JULER. On the two days preceding the meetings, four lectures were delivered at the Royal College of Surgeons by distinguished visitors from abroad.

Prof. A. FRANCESCHETTI (Geneva) spoke on cataract associated with lesions of the skin; Prof. G. B. BIETTI (Pavia) on ophthalmic aspects of protein deficiency and disordered protein metabolism; Dr. E. HARTMANN (Paris) on psychosomatic symptoms in ophthalmology, and Prof. H. J. M. WEVE (Utrecht) on ophthalmic manifestations of Besnier-Boeck's disease.

Having welcomed these and other guests, the President went on to announce that a medal for past and future Bowman lecturers had been cast. Sir John Parsons, F.R.S. (lecturer in 1924), Prof. Weve (1939), and Prof. Marc Amsler (1948) received the medal in person, and arrangements were made for its dispatch to Sir Arthur Keith (1930), Professor van der Hoeve (1932), and Dr. Arnold Knapp (1946).

PRESIDENTIAL ADDRESS

Two subjects considered in Mr. JULER's address were (1) the operation for acute glaucoma, and (2) refraction.

He paid tribute to von Graefe's pioneer work on glaucoma, which was achieved under the handicap of rudimentary anæsthetic technique, to say nothing of ignorance of the bacteriology of wound infection. He went on to point out the importance of avoiding trauma to the corneal endothelium, and emphasised the part played by this accident in producing anterior synechiæ. He contended that operation should not be unduly delayed after miotic drugs and other remedies have proved ineffective. In twenty-four hours—or in severe cases even less—the retina and optic nerve may be irretrievably damaged.

In refraction for objective estimation, he favours the use of a battery of spherical lenses in conjunction with a point-light or streak-retinoscope, and he spoke of the need for special accuracy in dealing with children. He also drew attention to the mistakes that may arise from tilting the lenses employed during retinoscopy, especially in cases of high refractive error, and described a method of avoiding such a source of confusion. For subjective testing he strongly recommended Jackson's crossed cylinders, and underlined the benefits from testing the binocular as well as the uniocular vision for distance. Chavasse's E-test was favourably mentioned, and comments were made upon the special problems of presbyopia, anisometropia, and oblique astigmatism. In connexion with oblique astigmatism Mr. Juler drew attention to the possibility of exploiting the compensatory ocular torsion which is noted when a patient tilts his head to either side. He ended by expressing his disbelief in the notion that myopia is provoked by using the eyes for near work. Heredity, he said, was the most important factor, though debilitating disease may sometimes play a part.

CORNEAL GRAFTING

A discussion on corneal grafting was opened by Professor FRANCESCHETTI, who gave a historical review of the subject and went on to say that minor differences in technique are not vitally important. Speaking on the relative advantages of keratectomy and laminated grafts, he deprecated the adoption of hard-and-fast rules. Every case presented a separate problem, and the question at issue was not simply which was the best method, but rather which one should be chosen in any particular case. Special consideration was given to the assessment of prognosis; and Professor Franceschetti admitted that the outlook is unfavourable in traumatic leucoma of the cornea and in aphakic eyes, whether or not the lens has been lost as a result of trauma.

Mr. J. W. TUDOR THOMAS (Cardiff) described his operative technique, with particular reference to cross-

Digitized by Google

suturing. He pointed out that the chances of a graft taking successfully are greater if the recipient cornea is opaque in the zone of implantation. Another feature to which he drew attention was the danger of vitreous prolapse if an operator tries, at the time of grafting, to remove the retrocorneal membrane often present in cases of old iridocyclitis.

Prof. G.-P. SOURDILLE (Nantes), part-author of the comprehensive report on corneal grafting issued last year by the Société française d'Ophtalmologie, reviewed the ways in which the fate of a graft may be jeopardised by associated ocular lesions and abnormalities of the eyelids. A small symblepharon, for instance, might be ignored, but extensive adhesions of the palpebral to the ocular conjunctiva necessitated a mucous-membrane graft before keratoplasty was undertaken. If there was reason to suppose that the lens was sufficiently opaque to preclude a good visual result from grafting of the cornea, then the graft should be completed before extraction of the lens, because aphakic eyes, as most authorities agreed, responded unfavourably to keratoplasty.

A film entitled *Trephine Keratoplasty* showed an operation for corneal graft, with successful outcome, performed by Mr. B. W. RYCROFT.

Mr. D. P. CHOYCE read a paper describing the technique and results of superficial lamellar keratoplasty in rabbits. These experiments, which were performed at the Institute of Ophthalmology, suggest that the grafted tissue in a successful case does not undergo rapid rejection. It seems to retain its identity until about six months later, by which time it falls due for normal replacement.

Dr. R. CASTROVIEJO (New York) briefly discussed the applicability of superficial and of whole-thickness grafts, and proceeded to show a series of extraordinarily clear colour-photographs depicting his operative results. Dr. J. I. BARRAQUER (Barcelona) showed a film which lucidly illustrated his technique of accurate apposition of the graft by direct suturing. Mr. G. W. BLACK (Leeds) described a case in which he had performed corneal grafting. Dr. A. FRITZ (Brussels) showed how a portable modification of the slit-lamp and corneal microscope can ease the operator's task, and he illustrated the way in which a contact glass may be employed for postoperative protection of the grafted cornea.

One of Professor Sourdille's collaborators in the French report on corneal grafting was Dr. L. PAUFIQUE (Lyon), who dealt with the three main indications for non-perforating keratoplasty. First, it may be employed as an optical device to improve the vision when a corneal opacity is confined to the superficial layers. Secondly, a superficial keratoplasty may prepare the way for a perforating graft when the latter procedure is contra-indicated by vascularisation of a dense leucoma. Finally, there are certain corneal conditions, including neurotropic lesions, which may be benefited by superficial keratoplasty. Dr. Paufique showed a film which clearly depicted his method of performing a peripheral lamellar graft.

Professor Bietti described his own modifications in technique, and gave a résumé of his results. He also referred to the possible advantages of administering vitamins and amino-acids to discourage the opacification of engrafted corneal tissue.

NEURO-OPHTHALMOLOGY

Dr. S. P. MEADOWS gave an interesting account of the symptomatology of internal-carotid aneurysms, and recounted several illustrative case-histories.

Discussing the problem of awareness or non-awareness of visual field defects, and cerebral metamorphopsia, Dr. MACDONALD CRITCHLEY paid special attention to the occurrence of optic alloæsthesia, in which objects appear to be displaced from one point of the visual field to the mirror-point on the opposite side. Another state of mind hitherto unfamiliar to most of Dr. Critchley's listeners was paliopsia, or visual perseveration, in which real objects extend themselves in time and space.

OTHER CONTRIBUTIONS

Mr. D. N. MATTHEWS surveyed the technique of plastic operations in the neighbourhood of the orbit. The subjects he considered were the treatment of congenital ptosis by a modified Blaskowicz operation, the correction of epicanthic folds, reconstruction of eyelids damaged by skin disease or trauma, the lining of a socket by mucous-membrane grafts, and reconstruction of the nasolacrimal duct.

Mr. J. R. WHEELER (Belfast) reviewed the effects of curare, retrobulbar procaine, and di-isopropylfluorophosphonate in reducing intra-ocular tension.

Mr. EUGENE WOLFF read a paper on normal and pathological ocular pigment, generously illustrated by histological pictures.

Dr. HARTMANN described his clinical experiences with Baillart's ophthalmodynamometer—an instrument used for estimating the pressure in the retinal arteries. Although admitting that this method has many limitations, theoretical and practical, Dr. Hartmann maintained that it is clinically valuable, so long as the technique is mastered and the results interpreted with discrimination.

Mr. W. J. WELLWOOD FERGUSON and Dr. A. G. MACGREGOR contributed an account of congenital colour-blindness associated with otosclerosis, and discussed the genetical aspects of this group of cases.

Dr. A. C. COPPER (Leiden) described the use of his orbitonometer for measuring the retrobulbar resistance in Graves's disease and other conditions.

Dr. G. KARPE (Stockholm), a pupil of Professor Nordensen, gave an account of his work on clinical electroretinography.

Some problems in ophthalmic dispensing were treated by Mr. J. PIKE; and Dr. J. HERKSON read a paper on retinal arteriolar spasm in toxæmia of pregnancy.

At the annual dinner on March 31 Professor Franceschetti proposed the toast of The Society, and the President replied. Dr. Macdonald Critchley and Lord Webb-Johnson replied to the toast of The Guests, proposed by Mr. J. H. Doggart. The President's health was proposed by Miss Ida Mann.

On April 1 a number of foreign visitors and their wives dined at Apothecaries' Hall as guests of the council of the Faculty of Ophthalmologists. They were welcomed by the president of the faculty (Sir Stewart Duke-Elder), and the honorary secretary (Mr. Frank Law) described the history and customs of some of the city companies and institutions.

Reviews of Books

Ernährungslehre und Diätetik

M. J. DEMOLE, reader in dietetics, University of Geneva; A. FLEISCH, director, physiology institute, University of Lausanne; CL. PETITPIERRE, reader in physiology in the university. Berne: Huber. 1948. Pp. 382. Sw. fr. 24.80.

THIS is the third of a series of volumes intended to cover all aspects of medical treatment. It has two main sections—a short preliminary survey of general principles, by Professor Fleisch and Dr. Petitpierre, and a much longer section, by Dr. Demole, in which the rationale o dietetic treatment is discussed and instructions are given for the appropriate diets. Dr. Demole is in charge of dietetic treatment at the Canton Hospital, Geneva and is well equipped to deal with this subject. It is however, a hard time for the planners of diets, even in Switzerland, and with fish and meat at 8 and 9 Swiss francs for one kilogramme some of the recommendations are sadly impracticable. One way in which the price of special diets can be reduced is by mass catering, and it is surprising that so little reference is made to the really excellent system of outpatient diet kitchens, supplying all meals at reasonable cost to patients, which is in operation in some of the biggest Swiss and American hospitals. Other subjects that might profitably have been given more space include the diets of infants and troubles arising from food allergy. The book contains a great deal of useful information, but much of it is scattered rather diffusely, and some regrouping of the tables might be considered for future editions. The index is somewhat perfunctory, and the doctor who has time to form his own opinion by consulting the literature would be glad if the references to the text of Dr. Demole's contribution were restored.

Digitized by Google

The Nomenclature of Disease

(7th ed.) Royal College of Physicians. London: H. M. Stationery Office. 1948. Pp. 385. 8s. 6d.

AT least three disease classifications have been published in the 18 years since the sixth edition of this Nomenclature appeared in 1931, and the delays arising from the war have led to the new volume appearing only a few months ahead of the World Health Organisation's international classification now obtainable in Geneva. This seventh edition differs considerably from its predecessor in arrangement, and the number of terms is well-nigh doubled. Some of its features show the influence of the American Standard Nomenclature, and in this the compilers pay tribute to a fine piece of work. An ætiological classification of disease is applied to the various parts and systems of the body in turn: well-known synonyms are included in brackets, and a separate list of eponyms is provided, though their use, with certain exceptions, is discouraged. A list of eponyms can never be complete, but this is undoubtedly one of the most comprehensive so far published. There is an index of over 17,000 entries—more than twice as many as before.

Some Common Psychosomatic Manifestations

J. BARRIE MURRAY, M.D., M.R.C.P., diagnostic physician, Tavistock Clinic, London. London: Oxford University Press. 1949. Pp. 114. 7s. 6d.

Dr. Murray contends that 60% of cases seen in a medical outpatient clinic are either wholly psychiatric or have an important psychiatric element. His clinical guide to diagnosis and prophylaxis will be appreciated by the conventionally trained practitioner. He examines in turn the cardinal symptoms and signs of effort syndrome, heads them off into the psychoneurotic fold, and enjoins an interpretation that can be followed by anyone familiar with the ideas of Babinski. The Service medical officer will be particularly grateful for the lucid descriptions of hysterical phenomena. A title more faithful to the author's material would perhaps have been "Common psychoneurotic manifestations simulating cardiovascular disease." Too much perhaps is made of a comparative analysis by percentages of the clinical features as they occur in psychoneurotic, effort-syndrome, low-backache, and heart-pain groups, whose members range in number from 15 to 400. On the psychosomatic side fever is not mentioned as being other than a precipitant of the syndrome; Friedman's papers (gathered together as *Functional Cardiovascular Disease*, 1947) on orthostatic giddiness and pulse-pressure, and on the mechanism of precordial pain, could usefully have been consulted. There are no references later than 1941.

Hematology

CYRUS C. STURGIS, M.D., professor of internal medicine, and director of the Thomas Henry Simpson Memorial Institute for medical research, University of Michigan. Oxford: Blackwell Scientific Publications. 1948. Pp. 915. 63s.

THIS large volume differs from other hæmatological textbooks in several ways. The most notable is the historical approach to all sections: this does not consist in a few early references, but involves an extended account of the early work and the development of our knowledge in every country, continued up to modern times. The later literature on this subject is immense, but the claim that a fair and careful selection has been made is, on the whole, justified. Another unusual feature is that no attempt is made to discuss in any detail the nomenclature and development of the blood and marrow cells: references to nomenclature appear in some chapters, but for the most part Professor Sturgis takes the reader's knowledge for granted; chapter 1 leads off at once with the classification of the anæmias.

The 23 chapters follow usual lines: the various anæmias, the hæmorrhagic diseases, the leukæmias, and so on are considered in turn. But each subject is dealt with in a more discursive manner, with more of a continuous argument, and with more of the author's own experience included, than is usual. This gives the book a distinctly individual flavour, and it is better written than many textbooks we could name. Separate chapters on sternal puncture and blood-transfusion conclude the volume. It is not well illustrated and the colour plates are indifferent.

The references suggest that this book was written some time ago; almost always the discussion stops short about 1943; and some of the chapters, such as those on hæmolytic anæmias and on iron-deficiency anæmias, are therefore of historical interest only. The work on folic acid, however, is described in an interpolated section.

The book cannot be recommended to students, for it assumes too much basic knowledge and is insufficiently up to date for higher examinations. It is much too long for the general practitioner, and clearly it is not designed as a work of reference. The person who will appreciate it is the practising hæmatologist, who will savour the finer points and the leisurely treatment of the subjects.

Change of Life in Women (London: Delisle. 1949. Pp. 76. 5s.).—Writing under the pseudonym of "Medica," a distinguished woman doctor gives an account of the menopause and its concomitants—hot flushes, moods, and minor disorders. She explains the physiology of the change of life and presents a reassuring picture of the whole process up to the stage when a new balance is achieved by the endocrines, and the woman settles down to the equilibrium which lasts her handsomely for the rest of what is often a long and useful phase of her life. Medica is not only informed in the disorders women experience at the menopause but is skilled in their alleviation; and her book explains clearly that most of them can be relieved, either by sedatives, reassurance, and a rearrangement of the woman's life and duties, or by suitable dosage with œstrogen. The book is always clear and is written with a sense of the turn of phrase which makes awkward topics acceptable. Not only the menopausal woman, but her family as well, and even her doctor, will profit by a glance through it.

The Scotsman's Food (Edinburgh: E. & S. Livingstone. 1949. Pp. 86. 3s. 6d.).—This "historical introduction to modern food administration," by Dr. A. H. Kitchin and Dr. R. Passmore, reviews, in a couple of hours' entertaining reading, the past and present diet of the Scots, and its relation to their health and social life. Written primarily for students, it could nevertheless be read with profit by many older people. Of the three chapters, the first describes the typical Scottish dietary from medieval times up to the 18th century: oats and barley, pulses, kale and cabbage, milk, cheese, and eggs, with potatoes and turnips as a latter-day addition, formed the staples, washed down with ale (not whisky). Meat and fruit were nearly always scarce, and fish dependent on local supplies. The effects of war, primitive farming methods, and drought on food-production are illustrated from contemporary accounts. Chapter 2 describes the "Age of the Industrial Revolution," when, in the middle of the last century, the population passed 3 million, which the authors regard as probably the maximum that could be fed off the country's own produce, however efficiently the land were farmed. The nutritional value of the common diet deteriorated through higher consumption of white wheat flour, refined sugar, and unvitaminised margarine, with a lower consumption, in the cities, of milk and vegetables. The crowding of people into slum tenements resulted in widespread rickets and appalling mortality among children: "the apparent industrial prosperity of the second half of the nineteenth century . . . was biologically a sham." The final chapter, on "The Age of State Planning," summarises the measures taken during and since the late war to ensure the equitable distribution of limited food-supplies. The authors do not underestimate the monotony of the Scotman's present diet, but they think it nutritionally adequate. They conclude that "probably never before in history, and certainly not within living memory, have the children of Scotland been so healthy. This is an achievement in which all those responsible for our war-time and subsequent food services may take justifiable pride."

The price of *Life and Sex* by Havelock Ellis was given incorrectly in our review (April 2, p. 570). It is published by Heinemann Medical Books at 17s. 6d.

Digitized by Google

THE LANCET

LONDON: SATURDAY, APRIL 16, 1949

Cryptogram of Age

"... man has aged considerably before he is born and continues to age rapidly in youth, and more slowly as life advances."

THIS pretty paradox of the laboratory, based on the rate of growth of tissues and their ability to reproduce themselves at the speed at which they themselves were formed, would hardly seem convincing to the old people in a chronic ward. Nevertheless, it reminds us, as Prof. A. P. THOMSON pointed out in his Lumleian lectures to the Royal College of Physicians last week, that we know very little about the process of ageing, even though we are beginning to know a little about the disorders of age. The first question is whether senescence is as inevitable as it seems. We know that its time of onset varies in different people, different families, and different races: it appears earlier in tropical races, for instance, than in those of temperate zones, which means perhaps that external environment, or the effects of infection, accident, malnutrition, or excesses, may hasten it. Moreover it is by no means universal throughout nature. Insects at death generally show no signs of antiquity, though some of them get a little tattered towards the end; fish have the laugh of us after all, for apparently they become neither senescent nor infertile; tortoises keep old age at bay for centuries; while perennial plants show no morphological evidence of senescence in succeeding years. Suitable modifications of the environment, indeed, may greatly prolong the growth period and survival of plants and seeds. Dr. THOMSON quoted, too, the findings of SAXTON that growing rats fed on a properly balanced but reduced diet lived much longer than a similar group whose diet was the same but unrestricted. Mature rats likewise lived longer when obliged to be abstemious; and this is a good argument, he thinks, for a moderate diet in middle age.

Even in the human body, ageing is not a uniform process: some organs keep their youth longer than others. The teeth, the joints (particularly of the vertebræ), the arteries, and the fat depots show changes long before the other organs; and possibly, Dr. THOMSON hinted, this early deterioration of the closed systems may be the result of metabolic or other disturbances conditioned from without. The life and reproduction of most cells can be prolonged by artificial culture for periods far exceeding the life-span of the parent organism; and cultures of aged tissue, though slow in starting, will grow as well as those from a young one. Their growth may be encouraged by tissue fluids from a young animal of the same species, which suggests that ageing of the tissues may have something to do with humoral changes. This seems to be borne out by some preliminary studies Dr. THOMSON and his colleagues are making at Birmingham. They have found some curious changes in the pattern of blood-chemistry in apparently healthy old men: the sodium and chloride are reduced, the hypoglycæmic response to intravenous insulin is delayed, storage of vitamin C is defective, and the excretion of 17-ketosteroids is diminished. He thinks these changes suggest a deficiency of the suprarenal cortex, but there is no increase in the blood-potassium and no clinical evidence of Addison's disease. The pattern of blood-chemistry is restored to the accepted normal by injections of testosterone, and on this treatment the patients gain weight and feel better. Another aspect of the problem of ageing is presented by progeria, and by the sudden appearance of senescence after mental or physical shock. In these latter cases the process is sometimes reversible, the grey hair becoming brown again, the wrinkled skin recovering its elasticity, and lost sexual desire returning.

Such facts, and the speculations they evoke, lead Dr. THOMSON to conclude that the more we consider ageing the wider is the field of research opening before us. "The problem," he said, "is one which intimately concerns the whole of clinical medicine, and yet has been almost entirely neglected." Moreover, what little we know is not being taught. "The virtual exclusion of the aged and the chronic sick from the wards of the teaching hospitals is responsible for serious defects in the training of medical students." The infirmaries at present are acting as acute general hospitals for the aged as well as caring for the hopeless cases. The aged sick should have the chance of being investigated at a general hospital. The danger of blocking acute beds with long-term cases can be overcome, he believes, by efficient classification; for the ultimate fate of the aged, he finds, can be determined within about three months of admission: some will die, some can be treated and sent home, and some will need protracted care in an infirmary. Under such an arrangement the long-term cases would be properly investigated and treated before they reached the infirmary wards. Undoubtedly the aged would gain if the responsibility for their care was shared in this way. As Professor THOMSON has shown, the problems they would bring to the general hospital would also enrich the main stream of medicine.

Cold Agglutinins

EVER since HAYEM discovered cold agglutinins in 1889, these antibodies have trapped unwary blood-groupers, who are liable to return as AB a blood that really belongs to some other group. These agglutinins are well known to be present quite often in the plasma of patients with various unrelated diseases—blood disorders like hæmolytic anæmia, aplastic anæmia and acute leukæmia; malaria, trypanosomiasis, atypical (virus) pneumonia, cirrhosis of the liver, and Raynaud's phenomenon. They are definite antibodies, found in the plasma. They agglutinate red cells best at a temperature of 3–4°C, and they do not act at all at 38°C; the upper limit at which they still act rises with the titre to which they can be diluted without becoming ineffective, and titres varying from 1 in 1 to 1 in 2024 have been

Digitized by Google

reported. The agglutination of red cells is characteristically reversed by warming to 38°C; the red cells absorb the agglutinins at low temperatures and release them again on warming. Cold agglutinins act on the red cells of all human groups, and when, in grouping, cells from a person with a cold agglutinin are added to the test anti-A and anti-B sera at room temperature, enough plasma is carried over with the cells to cause agglutination in both test sera, with the result that the blood is reported as of group AB. This pitfall can be avoided by the simple expedient of warming the mixtures; or alternatively the cells can be thoroughly washed in saline before testing. These precautions are all the more necessary since cold agglutinins are not confined to people with diseases: examining the plasma of 50 healthy persons ALLASIA,[1] in Rome, found them in 9; and the proportion was similar in 130 patients with miscellaneous illnesses. The possibility that a group-AB result may be due to cold agglutinins must therefore always be borne in mind.

BENHAMOU et al.,[2] in Algiers, have found cold agglutinins in 56 cases. The majority had malarial splenomegaly, but they refer especially to the presence of the agglutinins in hæmolytic anæmia with acrocyanosis, in acute hæmolytic anæmia due to sulphonamides, and in pregnancy.

Their patient with acrocyanosis was a man of 40, who even in Algiers had intense cyanosis of the nose, ears, and extremities; he also had a hæmolytic type of anæmia with an enlarged spleen. A strong cold agglutinin, titre 1 in 512, was found in his serum. When his hands were put into water at 37°C the cyanosis disappeared, but it returned when the water temperature fell to 33°C. By examining the nail-bed capillaries under a direct-vision microscope, agglutination of the red cells could be observed in vivo. The patient was then subjected to "l'épreuve des bains glacés," which not only caused him to turn blue but also raised his serum bilirubin and his excretion of urobilin. He was watched for a year and was found to be more anæmic in the cool season. As the cold agglutinins have been shown to be connected with the globulins of plasma (Cohn's fractions II and III) BENHAMOU et al. tried to desensitise their patient by giving a series of subcutaneous injections of his own plasma globulin. The effect was a surprising remission of signs and symptoms; the titre of the cold agglutinin fell to 1 in 4, and it ceased to be active above 20°C.

This combination of cyanosis in the peripheral vessels with cold agglutination has been noted before,[3] and BENHAMOU et al. are able to give a list of 15 recorded cases; but the treatment by globulin desensitisation is new and the results unexpected. Cold agglutinins have also been observed before in acute hæmolytic anæmias. BENHAMOU's patient had had a meningioma removed, and 46 g. of a sulphonamide drug was given in five days; in the anæmia which developed, and from which he died, cold agglutinins were present with a titre of 1 in 2024 against A and B cells and 1 in 512 against O cells. From experience with similar cases the Algiers workers suggest that a watch should be kept for the appearance of cold agglutinins in patients receiving large doses of sulphonamide, since they seem to herald the onset of hæmolytic anæmia and are thus a signal for stopping the treatment. As regards pregnancy the point they emphasise is that cold agglutinins occur even in seemingly normal persons, and that every apparent group AB should be checked in the manner described.

As might be expected, patients with cold agglutinins can be difficult subjects to transfuse, and BENHAMOU et al. describe some instructive cases.

One man, who belonged to group B and had a cold agglutinin of titre 1 in 4, was given some small transfusions of group-O blood, and after each of them had a severe reaction with cyanosis and pain in the spleen; there was no subsequent rise of his red-cell count. When he was given group-B blood there were only minor reactions and the transfusion satisfactorily raised the red-cell count. He was then transferred to the surgeons for splenectomy, and after the operation was transfused again—with group-O blood. When only 100 ml. had been given, he had a violent reaction and complained of constriction of the chest; "il est bleu de la tête aux pieds et glacé." Despite these vicissitudes, he recovered.

The lesson of such cases is that if there is a cold agglutinin in the recipient's plasma, compatible blood —matched at 37°C—of the recipient's group must be used. If the titre of the cold agglutinin is over 1 in 128, reactions must be expected and the blood must be administered slowly. Even with these precautions some patients will hæmolyse some of the transfused red cells. Here is one more reason for always giving blood of the patient's group instead of group-O blood; in this country, with its National Blood Transfusion Service, there is really no excuse, except in emergencies outside hospital, for the continued use of group O as the universal donor.

Toxicity of New Insecticides

SINCE we last commented on this subject,[1] a great deal of work has been done on the toxicity of the modern synthetic insecticides. STAMMERS and WHITFIELD [2] for example, have indicated that, used as an insecticide, D.D.T. is harmless to man and animals, but that risk to life may be incurred by unskilled formulation, by the use of unsuitable solvents, or by misapplication; and they emphasise the need to investigate the possibility of cumulative effects of storage in milk and in the tissues of sheep and cattle.

There are wide differences in the capacity of the various insecticides to produce injury through a single dose by mouth. As LEHMAN [3] has pointed out, the mean lethal dose ranges from 12,800 mg. per kg. body-weight for piperonyl butoxide to 2 mg. per kg. body-weight for tetraethyl-pyrophosphate (T.E.P), while D.D.T. comes roughly midway with a lethal dose of 250 mg. per kg. Thus the ratio is T.E.P., 125 : D.D.T., 1 : piperonyl butoxide, 1/50. The organic phosphate compounds and nicotine are extremely poisonous and rapid in action; the lethanes and thanite, while not so dangerous, have a rapid effect, producing collapse and death within a few minutes; while the chlorinated hydrocarbons, which include D.D.T., come next, with chlorinated camphene the most toxic, followed by the gamma isomer of benzene hexachloride (B.H.C. or 'Gammexane') and chlordan. The remaining compounds, including the pyrethrins and the insect activators N-propyl isomer and piperonyl butoxide, have so low an order of toxicity that there seems to be little

1. Allasia, G. *Policlinico*, 1948, **55** (sez. prat. 1109).
2. Benhamou, E., Zermati, M., Assus, A. *Ann. Méd.* 1948, **49**, 499.
3. See State, D., Wasserman, L. R. *Medicine, Baltimore*, 1943, **22**, 363.

1. *Lancet*, 1945, **i**, 248.
2. Stammers, F. M. G., Whitfield, F. G. S. *Bull. ent. Res.* 1947, **38**, 1.
3. Lehman, A. J. *Bull. Ass. Food Drug Officials*, 1948, **12**, 82.

Digitized by Google

risk from the ingestion of a single dose. The toxicity of 'Rotenone' varies greatly with species, but according to LEHMAN [3] no cases of poisoning have been reported in man.

The possibility of poisoning through the skin is particularly important to manufacturers and in connexion with spraying operations. STAMMERS and WHITFIELD have found that even gross exposure for many months to a 5% D.D.T./kerosene spray had no ill effects. "Neither of the writers can recall an occasion when the men did not return from a day's operations soaked to the skin with the 5% solution." On the other hand LEHMAN sees risk in multiple exposure to 9 g. per day, which is considerably less than that observed by STAMMERS and WHITFIELD. It is noteworthy that, with the exception of 'Parathion' and nicotine, all the insecticides that LEHMAN tested were more dangerous to handle in solution than as a wettable powder or as a dust. Even more important, repeated exposure increases the hazard to as much as 200 times that of a single exposure. Unfortunately, with almost all the insecticides tested, skin irritation was only slight to moderate, and thus gave little or no warning of impending danger. In the case of the organic phosphates this blandness towards the skin is especially disturbing; and the same group carries an additional hazard in that experiment suggests that a small drop of undiluted T.E.P. in the eye might prove fatal to man. Another serious possibility in dealing with some of the insecticides is that excessive quantities will be absorbed through the lungs as aerosols. STAMMERS and WHITFIELD, using D.D.T. continuous-phase aerosols under conditions of normal and supranormal insecticidal control, found no evidence of toxicity in man or animals, even with exposure up to three months, and this has been confirmed by laboratory workers using continuous-phase aerosols. People have now been exposed for upwards of three years to concentrations many times heavier than those in normal use, without ill effect. Goats similarly exposed have shown no symptoms, and we understand that bio-assay of their milk also gave negative results. But, if D.D.T. is apparently safe, very much less is known of the effects of many of the other insecticides in aerosol form; the possible hazards of chlordan, chlorinated camphene, benzene hexachloride, and the organic phosphates—to mention a few—can only be surmised.

Chronic poisoning can be incurred by eating vegetables and fruit contaminated by spray residues, and meat and milk from cattle that have fed on sprayed pasture or silage. Preliminary data suggest that there is little relation between acute and chronic toxicity: thus a rat cannot be killed by a single dose of gammexane, however large, yet it becomes grossly poisoned when fed with it, over a period, in concentrations as low as 10 p.p.m. On the other hand rats can safely ingest in the course of twenty-four hours a quantity of chlorinated camphene compound which would kill them in a single dose. The risk to man and animals from feeding on plants treated with systemic insecticides (in which the chemical is absorbed through the root system and insects feeding upon the plants are poisoned via the sap) is at present unknown, and great care will have to be exercised in their use. The translocation of parathion in plants, reported by LEHMAN, creates a new danger comparable to that of the systemic insecticides. Once absorbed by the human body, from any source, the toxicity of an insecticide will of course partly depend on its distribution in the tissues. Thus D.D.T. is stored in body fat at a level of from 4 to 10 times that of the dietary intake, while with gammexane the balance is about equal; but gammexane is said to have appeared in brain tissue—a finding unknown with D.D.T. Like the other chlorinated compounds, D.D.T. is also secreted in milk.

It seems fair to say that at present D.D.T. and gammexane, which are by far the most popular insecticides, are the safest under normal conditions of pest control by experts; but the cumulative effect of small doses has not yet been finally established. D.D.T. aerosols appear to be safe when used with reasonable intelligence. While the toxicology of all new preparations must be studied before they are brought into general use, it is well to remember that D.D.T. and gammexane are no more poisonous—and sometimes less so—than many of the older insecticides, fungicides, bactericides, and general antiseptics; examples are paris green, sodium fluoride, nicotine, hydrogen cyanide, the copper fungicides, and many of the more powerful antiseptics. The least toxic is not necessarily the safest, for large quantities may have to be used to control the pest.

The Budget and the N.H.S.

THE Chancellor's defence of his Budget was summarised in a single sentence. "The community as a whole," he said, "will enjoy extra benefits this year in extended social services and defence measures, and cannot, therefore, have them over again in the form of remission of taxation." He would be the last to fall into the error of supposing that the whole cost of the National Health Service is an addition to national expenditure; but the fact remained that hospital and medical services previously financed by the citizen as philanthropist or fee-payer now have to be financed from compulsory contributions and taxes. The strain thus thrown on the Exchequer led Sir STAFFORD CRIPPS to make the following significant statement:

> "There is . . . a very good argument for imposing some special charge or tax in connexion with the health services, both to help to finance them and to bring home to people generally the simple fact that they have to be paid for out of taxation. It is argued, with some force, that this might help to make people more economical in their use of the services. But, on the whole, I have come to the conclusion that we should await the outcome of another year before taking any such action, and I hope that there will be such economy in the use of the services as to make it unnecessary."

Actually there might be considerable advantages if the money for the National Health Service—or possibly for all the social services together—were raised separately: this practice would help to take these services "out of politics" and give them a degree of immunity from economy campaigns. Meanwhile it is clear that the Chancellor will not be readily persuaded to provide more than the £259,727,600 needed from the taxpayer to meet the estimated cost of the N.H.S. in the coming year (£352,324,600), and a Treasury circular says firmly that "except where necessitated by some special circumstances, for example a major change of policy, supplementary estimates will not be allowed." We trust that this will not be put forward as a reason for postponing the very necessary modification of the initial arrangements for the payment of general practitioners.

Digitized by Google

Annotations

A VENOUS SHUNT FOR MITRAL STENOSIS

Lutembacher's syndrome, as was indicated in our leading article of April 2, is the combination of mitral stenosis with an atrial septal defect.[1] With such a defect the acute attacks of pulmonary œdema and hæmoptysis commonly associated with mitral stenosis do not occur, because the increased pressure in the left auricle is transmitted through the defect to the right side of the heart; and the usual cause of death is right-sided failure. Moreover, the onset of auricular fibrillation is later in these cases than in those with mitral stenosis alone.

These observations led E. F. Bland, of Boston, to consider creating a similar shunt in patients with extreme mitral stenosis but good heart musculature who succumb from high pulmonary pressure—a state he terms "lung failure" in contradistinction to heart-failure. Since the heart, and especially the rheumatic heart, tolerates surgical intervention poorly, it was desirable that the shunt should be extracardiac. The surgical solution to this problem was provided by R. H. Sweet,[2] who in March, 1948, first anastomosed the azygos vein to the dorsal segment branch of the inferior pulmonary vein.

The patient was a girl of 17 who some years previously had contracted rheumatic heart disease. For nearly two years past she had suffered from attacks of severe orthopnœa and dyspnœa, mostly at the time of her menstrual periods; and during one of these attacks she had been admitted to hospital almost moribund with pulmonary œdema. On readmission to hospital she had clinical signs of a very tight mitral stenosis in a heart which was otherwise good and only slightly enlarged. The stenosis was so great that the added burden of increased blood-volume accompanying her normal menses was sufficient to precipitate an attack of pulmonary œdema.

The operation, which was not unduly difficult, served to show that a patient with such a lesion as this might safely undergo thoracotomy. The pressure in the left auricle was determined by introducing a needle into a pulmonary vein; this gave a water-manometer reading of 47 cm.—a figure at least four times the normal. In this operation special care has to be taken to avoid traumatising the pulmonary vessels, which are extremely tense with blood. Passive congestion in the lung segment deprived of its venous drainage, proved only transient. The dorsal-segment branch of the inferior pulmonary vein was divided as close to the right lung as possible. The azygos vein was then ligated and its distal end was anastomosed to the pulmonary vein by the tube method described by Blakemore and Lord.[3] At the end of the operation blood could be seen pulsating vigorously into the azygos vein right up to its junction with the superior vena cava. Convalescence was uneventful, the patient getting out of bed on the third day. So far, the operation appears to have been a success, since no further attacks of pulmonary œdema have accompanied the menstrual periods.

Sweet has performed this operation on 5 occasions; 4 of the patients show some improvement, and there has been 1 death. The patient who died had a high temperature after operation, with an increased blood-sedimentation rate; and the response to aspirin strongly suggested a recrudescence of her rheumatic fever. At necropsy a clot was discovered in the anostamosis; and this bears out what is probably the main criticism of the operation—namely, that it is a venous anastomosis. Arterial anastomoses are easier to construct and will stay patent, but with anastomoses between veins thrombosis is a likely complication. However, in these patients with mitral stenosis there is a big pressure gradient across the shunt. We understand that in the one case so far submitted to cardiac catheterisation after operation there was no substantial increase in the oxygen content of the blood in the superior vena cava.

This venous shunt represents a real advance, but it is suitable for only a small proportion of those suffering from severe mitral stenosis; and with it there is always a risk of reactivating an old rheumatic infection, which may have been apparently dormant for years.

1. Bedford, D. E., Papp, C., Parkinson, G. *Brit. Heart J.* 1941, **3**, 37.
2. Bland, E. F., Kelley, R. M. et al. *Amer. Practit.* 1948, **2**, 756.
3. Blakemore, A. H., Lord, J. W. *J. Amer. med. Ass.* 1945, **127**, 685.

CHILD AND YOUTH WELFARE THROUGHOUT THE WORLD

SOME of the non-political duties that the League of Nations used to perform have been taken over by the United Nations; among these is the publication of an annual report on child and youth welfare in various countries. The first of a new series [1] of reports on the progress of these services contains information sent in by 32 countries. Not all the reports are comparable, partly because they do not all cover the same ground and partly because standards range widely. Nevertheless it is interesting to note that the pattern of maternity and child-welfare work which this country helped to set out is being largely followed throughout the world, and that lately many of our views on the care of school-children and young people, deprived children and delinquents, are also gaining wide acceptance.

It is inevitable and right, however, that every country should interpret these services in its own way; and that sometimes public opinion, sometimes custom, and sometimes geography should influence the pattern. In Queensland, Australia, for example, an expectant mothers' correspondence service was established in 1944; this sends serial letters to expectant mothers in remote country districts, answers requests for special advice, and posts instructive booklets and clothes patterns. A "maternal and child railway car"—an ambulant child-welfare centre—journeys widely round the State, serving small towns and stations. In France, where children, and especially infants, suffered heavily from cold and hunger during the occupation, a unique service of wet nurses has been developed. Groups of wet nurses are enrolled in each area, and are trained for their duties and supervised by doctors. They serve either nurseries or private families, and the results, especially with State wards (many of them abandoned illegitimate children) have been so good that the establishment of centres was made compulsory in 1943. Some countries have established milk banks, and many—including Denmark, New Zealand, and New South Wales—have schemes to enable the unmarried mother to keep her child with her and to earn enough to rear him; in both these respects we are relatively backward, for we have very few milk banks, and our schemes to help the unmarried mother are inadequate and patchy. Family allowances have long been given in France and Belgium, and many countries besides our own have now followed suit.

Care of the deprived child varies, some countries relying chiefly on institutional care, others favouring foster care. The payment made to foster-parents is in some cases much more generous than is customary with us: in South Africa, it is stated, "specially generous grants are paid on behalf of children placed in this way,

1. Annual Report on Child and Youth Welfare. United Nations Department of Social Affairs, 1948. Lake Success, New York, U.S.A. H.M. Stationery Office. Pp. 236. 12*s.* 6*d.*

Digitized by Google

differentiation being made between normal children and those who present special problems of adjustment." This practice deserves attention, for though it may not be desirable to pay foster-parents on a scale which excites cupidity, it is right that the child's expenses should be fully covered, and perhaps that we should recognise that care of a difficult child is more exacting—and sometimes more expensive—than care of a normal one.

Treatment of delinquents is still very uneven; and our own system of children's courts, probation, remand homes, and approved schools, though far from perfect, is as promising as any. It is unfortunate, however, that the article contributed from the United Kingdom is largely a list of recent legislation and statute references, which gives no live picture of what is going on in our very lively social services. In Canada, the "juvenile and family courts" have proved their worth; these, while retaining the legal status of juvenile courts, have power to deal with a wide variety of family problems.

In our own country the State and the voluntary agencies share the work of maintaining social services for the child, though the State is accepting more and more responsibility. Other countries sometimes follow the same joint system and sometimes have a bias towards either State or voluntary care. In the Netherlands, for example, the government merely supervises, advises, and stimulates the voluntary bodies, to which it grants subsidies. Except in the large towns, social services are run mainly by the non-sectarian "Green Cross Society" and the Roman Catholic "White-Yellow Cross Societies." It would have been interesting if Russian experience could have been set alongside for comparison. The volume is otherwise an instructive Grand Tour of the world.

THE SEVERELY DISABLED ADOLESCENT

In Great Britain physically handicapped children with good wits generally get a fair start nowadays. But the intelligent child who is too severely disabled to attend a special school or to gain admission to a residential home not only gets a poorer start but has much worse prospects when he is grown. Nothing awaits him but a bed in a chronic ward, the company of old sick people, and a life almost completely devoid of interest and hope.

Some years ago the Shaftesbury Society, working with the Central Council for the Care of Cripples, opened a residential school at Hinwick Hall, Wellingborough, for 46 boys too seriously handicapped to be accepted in existing homes, and later the society opened a similar school for 45 girls at Malmesbury. Hinwick Hall receives boys of normal intelligence, between the ages of 10 and 16—cases of severe infantile paralysis, paraplegia with or without incontinence, spina bifida, hydrocephalus, cerebral diplegia, muscular dystrophy, osteogenesis imperfecta, renal dwarfism, and similar gross disorders. Some of the boys admitted have proved to be highly intelligent—well above the average—and have made good use of the excellent education offered at the school. Several have now reached and passed the age of 16, and the problem of what to do with them next has caused the society the greatest anxiety. In a few cases the Ministry has given permission for boys to be retained till the age of 19, but this has merely postponed the decision. A few can go home; but even where the home is good and the parents are willing, the care of these young people is work for skilled nurses. They must often be lifted, washed, helped on and off bed-pans, or given the assiduous care which alone can make life bearable for the incontinent. Their only hope of getting such care, or of getting something approaching it, is at present in a chronic ward. This has always been the fate of intelligent severely disabled adults; but these young people have the further trial that their minds have been trained to a relatively high educational level, and they need the companionship of educated and intelligent people of their own age. Inevitably, however, they must be scattered to the chronic wards maintained by their own local authorities. Even if they could be kept together their needs would only be half met. The society find that at 16 or 17 they become restive, unwilling to remain for ever at school, and anxious to be given some chance of earning a livelihood. This surely gives the key to the puzzle they present. It should be possible for them to graduate to another home—experimental at the outset—where occupational therapists could study their capabilities and suggest what remunerative work they might attempt. Many of the boys have, or could develop, special skills. One lad of 18 with osteogenesis imperfecta, permanently confined to a spinal carriage, has intelligence above the average, and draws well. It might be possible in such a case to provide work in lettering or sign-writing, and similar work might suit a boy with deformity of the feet and the right arm who is a good left-handed draughtsman. A boy with old infantile paralysis is good at his school work and above average mentally, but is becoming a behaviour problem because he has "had enough of school." His capacities would need special study because his disability makes him clumsy in writing. One or two boys have been fit enough to go on to ordinary training colleges for the disabled, but most are quite unsuitable physically.

These young people can only be a fraction of those in like case throughout the country; but even so the total number cannot be very great. Nevertheless their situation is so particularly cruel and hopeless that we feel special provision should be made for them, as soon as possible. Under the National Assistance Act and the National Health Act local authorities have permissive powers to further the interests of such people, as well as the duty of providing accommodation for them. Possibly an experimental training school could be set up by the Disabled Persons Employment Corporation; or, if a national undertaking of the kind is not possible just now, some of the great voluntary funds might perhaps be approached. The Shaftesbury Society does good work, but it is not a rich body, and would need the backing of others in this venture.

TREATMENT OF URÆMIA

In the last few years there has been increasing interest in the treatment of uræmia. One stimulus has been the clearer understanding, largely due to increased incidence, of a group of acute renal lesions termed by Lucke [1] the lower nephron nephroses, and typically seen with mismatched transfusion, ischæmic muscle necrosis, or mercury or other poisonings. A further stimulus is the development of dialysing methods—by the artificial kidney or peritoneal or intestinal irrigation—which enable the clinician to remove the retention products accumulated in the body owing to the failure of renal function.[2]

In acute renal failure the salient feature is necrosis of the lining epithelium of the distal convoluted tubules. Regeneration, which starts by the 8th day, may be expected to result in a continuous lining of debased epithelium by the 12th to 15th day. The ability of the kidney to excrete water returns with the regeneration of this epithelium; and if the patient can be tided over the anuric period renal function will slowly improve. Such manœuvres as decapsulation and splanchnic block cannot be expected to result in diuresis while the tubular epithelium is disorganised; it is in the removal of

1. Lucke, B. *Milit. Surg.* 1946, 99, 371.
2. Alwall, N., Norvilt, L., Steins, A. M. *Lancet*, 1948, i, 60. Annotation, *Ibid*, p. 221.

Digitized by Google

retained products during this phase that the value of any dialysing method must lie. Since the report by Frank, Seligman, and Fine[3] of the first successful peritoneal dialysis of an acute recoverable renal failure a large number of such cases have been treated by this method. Isolated cases cannot be readily compared, owing to differing techniques; but the account, by these same authors,[4] of 18 cases treated in this way should enable us to form some opinion of the method. Of their 18 cases, 12 had what may be regarded as recoverable kidney lesions; and 4 of these survived. Among the 4 surviving patients oliguria continued for 15, 7, 9, and 10 days. With this procedure the risk of peritonitis is very real, and indeed the authors conclude that at present the method "should not be considered for routine clinical use."

The treatment of 10 surgical cases with renal insufficiency has been discussed by Coller, Campbell, and Ieb.[5] Whereas the first 5 died, the last 5 survived; and in this second group the management was based on the "three-phase" treatment outlined by Muirhead.[6] The first phase is that of the actual period of kidney injury, which may be due to shock, intravascular hæmolysis, or a circulating kidney poison; the second phase is that of acute renal failure with oliguria or anuria; and the third phase comprises the recovery diuresis, during which excessive electrolyte losses may occur. The treatment of the first phase aims mainly at preventing kidney damage. In the second, or oliguric, phase the intake of water is restricted to the amount lost, which in the absence of vomiting or diarrhœa is estimated to be between 1000 and 1800 ml. per day. The five fatal cases were all treated by "forcing fluids." Lattimer[7] concluded from a study of 33 cases of urinary suppression that restriction of fluid intake below 2 litres per day during the oliguric phase is the most important factor in survival; and further impressive evidence for this belief has been put forward by several workers.[8] Unfortunately some reports on dialysing methods do not fully set out the ancillary treatment; and some of the credit given to the dialysis may really belong to fluid restriction. Further expert evaluation of dialysing methods is needed before these can justifiably come into routine use.

DIET AND DENTAL CARIES

FOR the last thirteen years Prof. Guttorm Toverud, of Oslo, has been investigating, first at Skedsmo and later in Oslo itself, the effect of health supervision, and of advice on diet, in preventing dental caries. In a lecture delivered in London last January and printed in the *British Dental Journal* for April 15, he explained that supervision was started in the antenatal period and was continued until the child was 7 years old. Expectant mothers were instructed by a dietitian in the choice and preparation of food for themselves during pregnancy, and for their children during infancy and the pre-school years. Natural foods, such as milk, meat, fish, whole-wheat bread, and fruit and green vegetables, were recommended in an endeavour to raise the daily intake of calcium to 1·6 g., of phosphorus to 2 g., and of iron to about 20 mg. The addition of one tablespoonful of cod-liver oil daily provided at least 7000 I.U. of vitamin A and 700 I.U. of vitamin D; and 15–30 g. of brewers' yeast was given to most of the mothers, together with extra vitamin C when this was considered necessary. From the age of one month the children were given two teaspoonfuls of cod-liver oil daily, and from the age of six months whole wheat as a breakfast cereal. The mothers were instructed that as soon as the teeth erupted, the children should end their meals with a raw vegetable or with raw fruit. The recommended diet contained only small amounts of sugar and refined carbohydrates. Vitamin K was given to all women during the last three weeks of pregnancy, and no instances of cerebral hæmorrhage were noted in any of their babies. The effect of this régime was to lower the stillbirth-rate and the prematurity-rate; there were fewer cases of rickets, and alimentary anæmia was rare.

In Skedsmo, the ages of the children examined ranged from $2^1/_2$ to 7 years; figures obtained during the war years have been excluded because of the general decrease in the incidence of caries during this time.[1] In the $2^1/_2$–3 years age-group supervision effected a statistically significant reduction in the number of caries-affected children, and there was a probable significant difference in the number of carious teeth; children aged 3–4 years also showed a significant difference in the number of carious teeth; but in those aged 4–7 years, the difference between the figures before and after the health supervision was not statistically significant. Unfortunately there has been a rapid increase in the incidence of caries in all the age-groups, especially the eldest. Similar results were obtained in Oslo; here the children attended from birth onwards, and the figures suggest that in pre-school children health supervision has the greatest effect when applied during the mineralisation period. Toverud does not believe it possible to name the factors responsible for this improvement in dental health, but he emphasises the importance in prophylaxis of eating natural foods and of restricting sweet foodstuffs; for, besides their action as a local factor, highly refined carbohydrates may lower good resistance built up during the pre-eruptive period.

Toverud's results are corroborated by Sognnaes,[1] who has analysed the war-time reduction of caries in European children. Surveying the period from 1909 to 1948, Sognnaes points out there was a definite decrease in the incidence of caries in the latter part of both world wars, and in the years immediately after; and also that there appears to be a delay of several years before the effect of war-time conditions on the teeth is observed. He has not discovered any uniform increase in the use of specific foods which could fully explain the reduction in the caries-rate, nor has he been able to show a real correlation between this reduction and lessened consumption of sugar; however, allowing for the time-lag, a correlation does exist. The lactobacillus count can be rapidly reduced by limiting the amount of sugar eaten,[2] but Sognnaes denies that this is the most important factor. He suggests that the improvement is brought about by the natural foods, which may actually contain a nutritional factor that benefits the teeth. In modern times it has been only during the two wars that the caries-rate and the consumption of refined carbohydrates have fallen towards the level of earlier days when caries was less commonplace than it is today.

AN impressive decline in European death-rates is recorded in the latest epidemiological and vital-statistics report from W.H.O. All but three countries now have a lower rate than in 1937–39. Among the countries for which data are available Rumania (21·1 per 1000) and Ireland (14·9 per 1000) had the highest rates in 1947. The Latin area of Europe, which before the war had rates ranging from 14 to 20, now has rates from 11 to 13 per 1000. The Netherlands still has the lowest rate in the world—8·1 per 1000 in 1947.

3. Frank, H. A., Seligman, A. M., Fine, H. A. *J. Amer. med. Ass.* 1946, **130**, 703.
4. Frank, H. A., Seligman, A. M., Fine, H. A. *Ann. Surg.* 1948, **128**, 561.
5. Coller, F. A., Campbell, K. N., Ieb, V. *Ibid*, p. 128.
6. Muirhead, E. E., Haley, A. E. et al. *Blood*, 1948, **3**, 101.
7. Lattimer, J. K. *J. Urol.* 1945, **54**, 312.
8. Humphrey, J. H., Avery-Jones, F. *Clin. Sci.* 1947, **6**, 173. Burnett, C. H., et al. *Surgery*, 1947, **22**, 994. Kugel, V. H. *Amer. J. Med.* 1947, **3**, 188. Strauss, M. B. *New Engl. J. Med.* 1948, **239**, 693.

1. Sognnaes, R. F. *Amer. J. Dis. Child.* 1949, **75**, 792.
2. Jay, P. *J. Amer. dent. Ass.* 1940, **27**, 393.

Digitized by Google

Special Articles

STUDIES OF CHILD GROWTH IN THE UNITED STATES

J. M. TANNER
M.B., D.P.M. Lond., M.D. Penna.
From the Sherrington School of Physiology, St. Thomas's Hospital, London

DURING the six weeks following the 1948 summer seminar in physical anthropology, held in New York City under the auspices of the Viking Fund, the generosity of the Fund made it possible for me to travel round the United States visiting various centres where child growth is being studied. The warm hospitality with which I was received enabled me to learn a great deal about the work of these institutes, and this article is concerned to pass on as much of this information as space permits.

Nowadays studies of growth are referred to as either *cross-sectional* or *longitudinal*. Cross-sectional study means the measurement at one time of several groups of children, one group aged 5 years, another 6, another 7, and so on. Such cross-sectional studies, like heart-lung preparations and decorticate cats, have their uses, particularly in the preliminary stages of research, but they tell us nothing about how much any one child grows, or about the variability of growth increments from year to year. A longitudinal study, on the other hand, enrols a hundred children at the age of 1 year, say, and follows each of the hundred till the age of 18. Pure longitudinal series are hard to come by for obvious administrative reasons, and some studies are a mixture of longitudinal and cross-sectional: children enter at various ages, continue in the study 5 or 6 years, and then drop out. The advantages of longitudinal studies, and the number of them completed and in progress, are such that most workers, when they use the term growth study, mean the longitudinal, or largely longitudinal, variety. All those here described are longitudinal.

COMPLETED STUDIES

University of Iowa

The first study of this sort in the United States was made by Dr. B. T. Baldwin, an educational psychologist, and published in 1914. In 1917 Dr. Baldwin was made director of the newly formed Iowa Child Welfare Research Station, of the State University of Iowa, and initiated anthropometric measurements as part of his routine study of the children attending the station. In 1921 he published his classical monograph, now unfortunately out of print, the Physical Growth of Children from Birth to Maturity as vol. I, no. 1, of the *University of Iowa Studies in Child Welfare*, a monograph series which is still one of the prime sources of information on child growth.

University of Harvard

Most of the older studies were initiated by schools of education, with emphasis laid on intelligence tests and scholastic performance as well as physical growth. In 1922 the well-known Harvard Growth Study began, directed by Professor Dearborn, of the Graduate School of Education. In sheer bulk this project far outdoes anything else in the history of growth studies. Measurements were made every six months of a group of school-children followed from the age of 5 years to maturity. The original group numbered no less than 3592, and at the end of twelve years, when the study closed, 970 were left. In 1939 all the original data were published; hence more or less complete records on nearly 1000 children are available. This study is mainly noteworthy, however, for providing the material for the masterly analysis of growth at adolescence by Dr. Frank Shuttleworth, whose papers will be found in the Monographs of the Society for Research in Child Development.

University of California

The Institute of Child Welfare, University of California, was founded in 1927 and is directed by Prof. Harold Jones, a psychologist. It houses three separate growth studies, each of which ceased collecting data a short time ago, though more publications from them can be expected for many years yet.

(1) The Berkeley Growth Study, run by Dr. Nancy Bayley, initially had some 30 boys and 30 girls at birth, of whom 20 of each sex remained with the study till maturity. 22 physical measurements were taken at the usual intervals (monthly the first year or so, then three-monthly for a few years, then six-monthly), with front-, side-, and back-view photographs, radiograms of hand and knee, and a considerable number of psychometric tests. Several of Dr. Bayley's papers will be found in *Child Development*.

(2) The Child Guidance Study, directed by Dr. Jean Macfarlane, was mainly a psychological and sociological study, with detailed records of behaviour and attitude of children and parents for some hundred boys and hundred girls.

(3) The Adolescent Growth Study concerned some 70 boys and 70 girls followed from the age of 9 years to that of 17. Measurements were made and photographs taken, but this study is chiefly remarkable in that it was deliberately physiologically oriented, under the direction of Dr. Nathan Shock. Dr. Shock's papers on the relation of adolescence and menarche to blood-pressure, basal oxygen consumption, heart-rate, exercise-tolerance tests, and creatine excretion will be found partly in the usual growth journals already mentioned and partly in the *American Journal of Physiology*. In addition a monograph has been published by Dr. Anna Espenchade on motor performance in adolescence, and a book by Dr. Harold Jones based on longitudinal records of strength and associated physical data is now in the press, and another by Dr. H. Stolz on adolescence in boys is awaiting publication.

Western Reserve University

The Brush Foundation Study at Western Reserve University was begun in 1931, ceased in 1942, and was directed by Prof. Wingate Todd, an anatomist and physical anthropologist. It had an enrolment second in size to the Harvard Growth Study, of 575 boys and 484 girls, but was only semi-longitudinal; the children entered at various ages, and on the average continued only $4^1/_2$ years with the study. The total age span covered from 3 months to maturity. No less than 25 anthropometric measurements were taken, besides radiograms of the hand, foot, elbow, knee, and shoulder. These pictures were the basis of the Todd standards for skeletal maturity, which are perhaps, in their revised edition, still the best known of the various methods of assessment of skeletal maturity available to pædiatricians. In the same department was housed the Bolton Study of craniofacial development, in which, among other things, lateral radiograms of the head were made, which have been used by Dr. Earl Count in 1942 and Dr. Carl Francis in 1948 for studying the growth of the skull and the pituitary fossa respectively. Both these papers are in *Human Biology*, another journal which carries a considerable proportion of papers on human growth.

STUDIES IN PROGRESS

Having now mentioned the main, though by no means all, completed growth studies, we will turn to four chief projects which are still in progress, and likely to remain so indefinitely. Three of the studies in progress are directed by pædiatricians—the emphasis has swung in this direction in more recent years—and the fourth is the Iowa Child Welfare Research Station, which still continues a programme of physical measurement, in addition to psychological studies and some physiological ones.

Digitized by Google

University of Iowa

Dr. H. V. Meredith is now in charge of physical anthropology, and at present is engaged in two projects. A fairly extensive series of anthropometric measurements is being taken at six-month intervals from the age of 4 years to maturity in a series of children who, it is hoped, will yield eventually 75 of each sex followed uninterruptedly. Particular emphasis is being laid on accuracy of measurement, and all measurements are made by two observers whose figures are checked if they do not agree to within established standards of tolerance. In addition Dr. Meredith is collaborating with the staff of the Dental College in a study of facial growth in about the same number of children, using radiograms, direct measurements, casts, and standardised photographs.

University of Colorado

The Child Research Council of the University of Colorado, at Denver, was founded in 1927 and has at present 130 children coming from 88 families. About 6 new children are enrolled every year, half or more of them being usually siblings of members. Members join as soon after conception as knowledge permits, and there are more mothers applying spontaneously on their behalf than can be accommodated. The earliest members are now mature, and second-generation children, those of enrolled parents, are beginning to enter. The morphological, physiological, and psychological growth of these persons is studied throughout their life, particularly during childhood, the emphasis being placed on the synthesising activity of "understanding the child himself as a whole integrated living organism."

The director of the study is Dr. Alfred Washburn, and the staff includes 8 M.D.s and 6 PH.D.s or the equivalent. Relations with the medical school in the University (where the study has the title of Department of Human Growth) are closer than is the case with any of the other child-growth institutes. In the departments of anatomy, pathology, biochemistry, and clinical biochemistry one of the full-time salaried members of the Child Research Council staff works on a permanent basis; all child pathology is controlled by the C.R.C., and several members, including the director, actively teach on the pædiatric faculty. Recently an introductory freshman course covering the broad principles of human biology has been instituted in the medical school, and the C.R.C. has the responsibility for a quarter of it. The majority of publications have appeared in pædiatric journals, and are strongly clinically oriented.

At present some 20 anthropometric measurements are taken, with front-, side-, and back-view photographs. A very considerable amount of radiographic work, partly clinical and partly anthropometric, has been done by Dr. Marion Maresh. Growth of the limb bones, lungs, and paranasal sinuses is being studied, and the data on the lengths of humerus, ulna, radius, femur, tibia, and fibula are probably the most reliable for these dimensions yet assembled.

There is a considerable physiological programme too, embracing basal metabolism, blood-protein levels, hæmatology, electrocardiograms, reaction times, vital capacity, and an exercise-tolerance test. One of the members of the staff is a nutritionist and food-intake assessments are being made, together with some studies of blood-vitamin levels. There is an orthodontic study under a dentist's direction, and both mental testing of the familiar intelligence type and behaviour study and projective and psycho-analytic work under the direction of Dr. Benjamin.

Fels Institute, Antioch College

The Fels Research Institute for the Study of Human Development began in quite a small way in 1929, but it has continuously expanded since, until now it is by a considerable margin the largest of American growth-study institutes, in terms of physical facilities and its annual budget. This year the institute has moved into a new specially constructed building, Fels House, which like the old accommodation, is on the campus of Antioch College in Yellow Springs, Ohio. Fels House has 78 rooms, including a large biochemistry laboratory, several small and one large air-conditioned physiological laboratories with elaborate electrical room-to-control-room leads of the familiar conditioned reflex study type, a radiography room with ten different radiographic measurement set-ups arranged round a central track for the tube, two anthropometry rooms, medical and dental examining-rooms, several nurseries and observation rooms, a library, an auditorium, and (outside) an animal-house.

The study has some 210 enrolled children, from about 130 families, and aims to study them from fœtal life to maturity in the morphological, physiological, and behavioural fields, with particular emphasis on the borderlines between these fields and on the constitution and genetics of the children. The series includes 3 sets of triplets, 6 pairs of twins, and many siblings. About 12 new children are added every year, and about half of these represent new families. As in the University of Colorado study, no difficulty whatever is encountered in obtaining subjects. The director of the study since its inception is Dr. L. W. Sontag, and the staff includes 3 M.D.s and 6 PH.D.s with genuinely adequate secretarial and technical help.

The physical anthropology section, directed since 1943 by Dr. Earle Reynolds, in addition to the usual anthropometry and photography makes very extensive use of X rays for measuring. The usual type of films are taken of every part of the body every six months, and in addition from the age of $6^1/_2$ years onwards special films are made to delineate subcutaneous tissue, bone, and muscle. Eight areas of body and limbs are radiographed, small strips about 2 in. being taken, for example, across the greatest circumference of the calf. Publications have so far dealt with growth of the pelvis, tissue analysis of the calf region, seasonal factors in growth, physical changes at adolescence, methods for analysing growth progress, and biochemical-structural relationships. Dr. Reynolds intends very soon to publish a comprehensive account of the subcutaneous tissue in the various regions.

The physiological-biochemical programme is on a considerably greater scale than that of any other study. Dr. John Lacey, in charge of physiology, is chiefly occupied with cardiovascular, respiratory, and palmar-sweat responses to a stress of the cold-pressor-test type, with special relation to whether the different responses observed in different children are relatively constant for each child, or changed by ageing or by environmental changes. Studies of fœtal reactions are also being made. Dr. Leland Clarke, in the biochemistry section, is concerned chiefly with creatine, creatinine, cholesterol, blood enzymes, and steroid metabolism, and has been developing methods of micro-analysis appropriate for obtaining determinations of several different chemicals from a single finger-prick on a diffident child. Nutritional studies are being made, and there is a large psychological-sociological department under Dr. Alfred Baldwin.

University of Harvard

The Centre for Research in Child Health nd Development at the School of Public Health, arvard, was opened in 1930 under the direction of Prof. H arold Stuart. The arrangement of the centre and its meth ds have been described in the Monographs of the Society for Research in Child Development in 1939, and some f the results in later numbers of the same and other j urnals. The original plan was to obtain complete longitu inal records

Digitized by Google

from birth to maturity in 100 boys and 100 girls. By 1937, 224 out of an initial 296 children were still being examined at regular intervals, and further recruitment was stopped. From 1941 to 1944, however, the work of the centre was considerably disrupted and for 1½ years practically ceased. About 150 of the original group of children are still under study, the oldest now aged 17 years and the youngest about 12 years. The staff of the centre has varied from time to time, but before interruption was about 4 M.D.s and 2 PH.D.s, besides some part-time and consultant helpers.

The centre has always been strongly medically oriented, and follows physical growth, nutrition, health history, and behaviour. Eighteen anthropometric measurements with photographs, and radiograms suitable for the differentiation of subcutaneous tissue, muscle, and fat, have been taken from birth. These radiograms constitute the most complete set over this age range ever assembled, but as yet only the calf plates have been fully analysed. Standards of skeletal maturity based on these films are being prepared and are soon to be published. Detailed dietary histories are also available, both of the mother during pregnancy and of the child followed from birth to adolescence.

Though little physiological work has been done in the centre itself, various outside investigators in the Boston area have used these children for studies on basal oxygen consumption, creatinine metabolism, hormone excretions, and the like. The centre also participated in the morphological and physiological work involved in the now concluded growth study of the psychological clinic of Harvard University, the results of which were published by Dr. R. N. Sanford and his associates in 1943. This latter study is mainly psychological but includes considerable data on the interrelations of morphological, physiological, and psychological variables.

CONCLUSION

These are a few of the main things going on in the main growth studies in the United States: the reader should not imagine that he has obtained from this short article a detailed or complete view of all that is in progress. A longer report, which lists 7 continuing and 9 now closed studies, will be found in the 1947 *Year Book of Physical Anthropology*, but even there the ground is but partly covered. The volume of this work and the excellence of a large part of it is an inspiration and a guide to those here who are in a position to emulate and enlarge on it; a source of many data for those whose interest is not matched by their facilities for collection of their own figures; and a stimulus to all biologists of whatever variety who realise the overwhelming importance of form, and the seemingly overwhelming problems raised by it.

I want to thank most sincerely all the investigators I visited for the time and trouble they took to show me all the workings of their laboratories, and particularly Dr. Carrol Palmer, Dr. Paul Sawin, Dr. Frank Shuttleworth, Dr. Edith Boyd, Dr. Howard Meredith, and Dr. Earle Reynolds for their hospitality.

BIBLIOGRAPHY

The main journals in which papers on human growth are published are those referred to in the text, the *American Journal of Physical Anthropology*; *Growth*; the *Journal of Pediatrics*; and the *American Journal of Diseases of Children*. Starting-points in the literature of the studies referred to above are: *J. consult. Psychol.* 1939, **3**, 157, and *Child Develpm.* 1943, **14**, 1, for the University of California study; *Monogr. Soc. Res. Child Develpm.* 1944, **10**, no. 1, for the Brush Foundation study; *Growth* (1947) **11**, 1, for the Iowa study; *Amer. J. Dis. Child.* 1943, **66**, 227, and *J. Pediat.* 1937, **11**, 37, for the Denver study; *Child Develpm.* 1947, **18**, 130, for the Fels study; *Monogr. Soc. Res. Child Develpm.* 1939, **4**, no. 1, for the Harvard School of Public Health study; and *Amer. J. Roentgenol.* 1947, **57**, 477. Behind these lie W. M. Krogman's *Bibliography of Physical Anthropology* and his article in *Tabul. biol.* 1941, **20**, and *Child Develpm. Abstr.*

MALIGNANT DISEASE OF FEMALE PELVIC ORGANS

CONFERENCE AT NEWCASTLE

A Conference on Gynæcological Cancer, organised by the departments of gynæcology and radiotherapy of the Royal Victoria Infirmary and the Medical School, King's College, Newcastle-on-Tyne, was held on April 1–2, attended by 133 gynæcologists and radiotherapists.

CARCINOMA OF THE CERVIX

Prof. E. FARQUHAR MURRAY (Newcastle) presided when Mr. VICTOR BONNEY gave the introductory address published on p. 637. At the conclusion Mr. Bonney received an ovation from more than 250 people who had gathered for the occasion. At the evening session Sir WILLIAM GILLIATT, P.R.C.O.G., took the chair.

Mr. MALCOLM DONALDSON (London) spoke of the improvement in the results of the radiological treatment of cancer of the cervix; but he said that, whereas there had been a marked improvement in cases in stages 1 and 2, the figures for stages 3 and 4 remained the same as ten years ago. Even with the improvement, about half the cases in stages 1 and 2 did not survive five years. He was now convinced of the value of the Glucksmann-Spear technique of estimating radiocurability, and he advocated the use of the Bonney-Wertheim operation in those cases which were not radiocurable. In stages 3 and 4 a better distribution of radiation was required for adequate treatment. He described the Neary applicator and mentioned some of the difficulties encountered in its use.

Mr. GEORGE BLOMFIELD (Sheffield) gave a detailed account of the uses of radium and X rays in cervical carcinoma and described his own cervical applicator.

Mr. DAVID CURRIE (Leeds) said that his interest in the subject had been aroused at the beginning of the war, when radium was difficult to obtain because of the risk of air-raids and he was consequently forced to use surgery. He had performed Wertheim's operation 71 times, without an operative death, and 2 of his patients already had ten-year cures. He selected cases in stages 1 and 2, and most of his patients received preliminary irradiation.

In the discussion that followed, both Mr. BONNEY and Mr. DONALDSON called for greater coöperation between gynæcologists and radiotherapists, and Mr. JOHN THURGAR (Newcastle) pointed out that gynæcologists and radiotherapists in Newcastle had collaborated very closely for many years now. Various speakers indicated their desire for "individualisation"—the employment of the most appropriate methods of treatment in each case.

Mr. STANLEY WAY (Newcastle) announced that, in view of criticisms of the accuracy of staging, made to him by Mr. Bonney, he had invited two gynæcologists and two radiotherapists to examine four untreated cases of carcinoma of the cervix under anæsthesia, and to stage them. Except in one case, not more than two observers had agreed on the staging, and when the description of the extent of the tumour was examined there was even greater disagreement.

Sir WILLIAM GILLIATT, in concluding the discussion, said that he was glad to see that the need for greater

Digitized by Google

team-work was being realised. He thought that the new radiotherapy advisory committee set up by the Minister of Health would facilitate coöperation.

OTHER TUMOURS

On April 2 when Sir WILLIAM FLETCHER SHAW (Manchester) presided, Mr. ALAN BREWS (London) spoke on *chorionepithelioma*. He cautioned his hearers on the interpretation of the Aschheim-Zondek reaction and pointed out that positives in a dilution of 1 in 100 occurred about the 60th day of normal pregnancy and even later in multiple pregnancy. But when the diagnosis of chorionepithelioma was established radical treatment was necessary, even though the patients were very young or had remote metastases, provided (in the latter case) that the patient's general condition was good. He showed that metastases sometimes disappear spontaneously.

Dr. ALFRED GLUCKSMANN (Cambridge) spoke of the rôle of the tumour bed in the *treatment of squamous carcinomas by irradiation*. He said that the tumour bed at the primary site played a major part in the response of the tumour to irradiation. The stromal reaction induced by the tumour at the site of its metastases was essentially the same as that occurring at the primary site, and in carcinoma of the tongue it had been found that the response at the primary and secondary sites, when both were full irradiated, was essentially the same.

Mr. HARVEY EVERS (Newcastle) read a paper on the clinical aspects of *malignant ovarian tumours*. He showed that 82% of all these tumours occur after the age of 40 and said that when an ovarian tumour was found after this age there were almost equal chances of its being benign or malignant. He thought that tumours at such an age might well be treated radically by hysterectomy and removal of both ovaries even if they did not appear malignant. He pleaded for a wider adoption of the method of staging these tumours, so that uniformity between clinics could be achieved. He thought that postoperative deep X-ray therapy should be employed experimentally until there was definite evidence of its value or otherwise.

Dr. C. W. TAYLOR (Birmingham), in a paper on the pathology of malignant ovarian tumours, called for a simpler classification than those existing at present, which, though perhaps histologically accurate, were rather bewildering to the clinician. He discussed the bearing of the histological picture on the ultimate results and recorded an over-all five-year survival-rate of 15·5%. He described his method of grading on which prognosis could be based, and said that the best results could be expected in the cystic type of tumour.

DEMONSTRATIONS

At a clinical demonstration given at the Queen Elizabeth Hospital, Gateshead, by members of the staffs of the Newcastle hospitals, under the chairmanship of Sir EARDLEY HOLLAND, unusual and interesting specimens were shown by Messrs. EVERS, STABLER, SNAITH, ARTHUR, THURGAR, and WILLIAMSON and Drs. TROUNSON, RANNIE, and GLUCKSMANN. Mr. Thurgar and Dr. Farmer described and showed a radium applicator for treating carcinoma of the vagina, and Mr. WAY showed some of the late results of the extended radical operation for carcinoma of the vulva and some examples of massive surgical resection for advanced pelvic cancer, including extirpation of a recurrent ovarian carcinoma with excision of the rectum, and two cases of carcinoma of the cervix successfully treated by Wertheim's operation with total cystectomy.

The conference concluded with a visit to Durham, where members were shown over the Cathedral by the Dean, and a dinner was held in the great hall of Durham Castle.

THE BLOCK AND THE STUDY-DAY

AN APPROACH TO STUDENT STATUS FOR NURSES

GOOD training attracts good students. The steady and increasing flow of young educated women into the social services and physiotherapy can be partly explained by the fact that training for these callings is stimulating, well planned, and devised entirely to fit the student for later practice. In nursing, on the other hand, training is subordinate to the needs of the hospital; and as long as we continue to nurse our sick very largely by student-power it will remain so. All hospitals pay lip-service to the ideal of student status for nurses; and a few even try to achieve it. This is not easy to do, for nursing is a practical art, and the custom of giving the student plenty of experience with patients has more than convenience to recommend it. Moreover, recent studies have shown that trained staff, too, are scarce in hospitals; nurses who have taken their qualification do not jostle each other for hospital appointments. There is thus little chance at present of increasing the ratio of trained staff to students.

The joint burden of theory and practice, however, has always lain heavily on students, and liberal-minded matrons nowadays try to ease it in one of two ways —by the block system, or by the weekly study-day. The advantages and drawbacks of these two methods deserve consideration, for in some ways they rival each other.

A TERM OF THEORY

Good examples of the block system were described in the *Nursing Times* of April 19 and Nov. 6, 1947. In one of these, a large London teaching hospital, the student begins with 12 weeks in the preliminary training school, followed by a week's holiday; she then has 9–10 months in the wards followed by her first annual holiday, presumably of 3 weeks or a month; early in her second year she has a 6-week period (or block) of study only, and then continues with ward experience until she gets her second-year holiday; the third year *begins* with a 6-weeks' block, and shortly before her final examination she gets a last block-period lasting a fortnight. During the blocks nurses work a five-day week; so in the course of three years' training, they get 130 days free of ward work and dedicated purely to study. The *Nursing Times* says:

> "They are treated like students. They have breakfast at 7.20 and begin work at 8.30 A.M., finishing either at 4.30, 5.30, or 6 according to the programme, but having one afternoon free for shopping during the week. They have the weekend free from 12 on Saturday till Sunday night."

The second large general hospital has a similar system except that the blocks and holidays are arranged—and this shows that it can be done—so that the nurse always has a holiday before going on night duty, and is always on day duty or attending a block before she takes an examination. Counting the preliminary training school as a block, she gets 16 weeks of study in the first year, 8 weeks in the second year, and 8 weeks in her third year—160 study-days in all. In this hospital the nurse "on the block" breakfasts at 6.30 A.M. and goes on the wards from 7 to 8 A.M. She begins her study-day with a test paper at 8 A.M. and she finishes it at 5 o'clock in the afternoon.

In criticism of both schemes we must point out that students in no other discipline would be expected to begin a study-day so early; or to attempt a span of brain-work lasting 9 or 10 hours. University students usually reckon they have done a good day when they have completed 6 hours of brainwork. Again, though there are good arguments for keeping the nurse in touch with the wards during the block period, it is

Digitized by Google

wasteful to use her morning freshness on routine chores. The custom of sending her on the wards from 7 to 8 A.M. began in this hospital when staff were too few to manage the work of that busy hour. That reason no longer holds, but the custom is unfortunately maintained. The nurses would certainly benefit physically and mentally by getting an extra hour of sleep in the mornings of the block period, and perhaps also by having an hour's clinical work later in the day when it would make a refreshing break in their studies.

PRACTICE INTERSPERSED WITH THEORY

The alternative to the block system—the weekly study-day—also has much to recommend it, and again two examples may be quoted.

In a large London teaching hospital nurses spend 11 weeks in the preliminary training school, and then enter the wards. After entering the wards they have two courses of weekly study-days yearly, beginning in March and September. They get 16 study-days in the first year (two 8-week courses), 17 in the second year, 16 in the third year and 4 days in preparation for the final examination—53 days in all, or counting the preliminary training school, 108 days.

In the second example, a large general hospital, the preliminary training school course lasts only 8 weeks; this is a matter of principle: the matron believes that students learn more easily, and retain their keenness better, if they are taught only nursing measures in the preliminary training school, and are not taught anatomy and physiology until their curiosity about the structure and function of the body has been aroused by a little ward experience; and there is much to be said for this view. They have two 12-week periods of weekly study-days in the first year, in addition to the 8 weeks in the preliminary training school. In their second year they get one period of 8–10 weeks, and a like period in their third year. Study-days in the three years' course at this hospital thus range from 8 to 84—which compares poorly with the 130 or 160 days of nurses trained on the block system.

FROM THE STUDENT'S VIEWPOINT

The nurse allowed only 4 days to rub up her knowledge for the final must surely think enviously of the girl who gets a fortnight; while the average nurse—who gets no extra time at all—must think bitterly of both. When the vast area covered by the theoretical syllabus is considered, it is impossible to see how any ordinary young person could master it in 160 days, let alone 80; and this explains why examiners of nurses so often set difficult questions but mark them on a low standard: no other course is open to them.

The block system, since it keeps the nurse for some weeks out of the run of the tide in the wards, is said to divorce theory and practice. It is also difficult to arrange administratively, requiring more additional nurses than the weekly study-day and being altogether less flexible. If a nurse falls sick while taking a block period it is difficult to fit her in again to make up lost ground; but on the other system, the nurse can either make up the lost ground with the sister tutor, or join the next group when they are taking the lectures she missed. Moreover she remains in touch with her cases, and is even called upon to demonstrate one from time to time on a study-day. The whole week is the lighter for being broken by a study-day in addition to the day-and-a-half off duty; and matrons are somehow more humane about arranging the study-day than they are about planning the block.

In one of the hospitals quoted the nurses do not breakfast on their study-day till 9 or 9.30 A.M., and come to their first lecture at 10.30; they can even sleep out the night before if that happens to be their day off. Formal work ends at 6 P.M. and they have the evening free for private study. At the other hospital, study-day lectures begin at 9 A.M. and the day ends at 4.30 P.M. Thus the nurses get up later on two mornings a week (the day off and the study-day)—which is good for young people who may have contracted a sleep-debt. They also say they have a sense of continuous study with no cramming.

The drawback to the study-day system is that it only covers 8–16 weeks in the second and third years. Nurses questioned own that they wish it went on all the year round, but the various courses occupy 8 months of the sister tutor's year, leaving 4 months clear for the holiday seasons and for the time spent by students on night duty. Perhaps the solution would be to allow 2 study-days a week for selected short periods during the three years' course.

Whatever the rival merits of these two systems, they are both an outstanding advance on the still general custom of forcing the nurse to study in whatever odd moments she can find. They are a genuine attempt to give her some of the privileges of a student, and to offer young people entering the profession some of the status and consideration extended to those entering the medical auxiliary and social services. Headmistresses and others who know the young educated girl say that good training will always attract her. If matrons generally would adopt one or other of these systems—and do it in a realistic spirit, recognising the nature of the world we live in, and the girls they are seeking to attract—they might go far towards ending the grim situation in which shortage of student nurses has placed us.

REGIONAL HOSPITAL BOARDS

THE Minister of Health has made the following appointments to fill the vacancies caused by the retirement of a third of the members of the 14 boards in England and Wales. Out of 118 appointments so far made, 87 are reappointments of retiring members. There are still 8 appointments outstanding. Those now appointed will hold office till March 31, 1952. The names of members of the medical profession are shown in bold type.

NEWCASTLE REGION

Reappointed: Thomas Benfold, C.B.E., J.P.; E. F. Collingwood, C.B.E., J.P.; Alderman Alfred Cooper; **D. C. Dickson,** F.R.C.S.E.; John Foster; **William Fraser,** M.B.; Alderman J. A. Hutchinson; Robert Muckle.

New member: Rev. R. E. Robson. One further appointment still to be made.

LEEDS REGION

Reappointed: Alderman H. J. Bambridge, O.B.E., J.P.; Lawrence Crowther, O.B.E., J.P.; Miss M. F. Dykes, S.R.N.; **D. C. Muir,** F.R.C.P.; Prof. **Matthew Stewart,** F.R.C.P.; Alderman Arthur Sugden, J.P.

New members: A. F. George; **W. W. A. Kelly,** M.B., J.P.

SHEFFIELD REGION

Reappointed: Alderman C. F. Bowmer, J.P.; **J. W. Brown,** F.R.C.P.; A. W. Harrison; Lord Quibell, J.P.; Alderman Edward Sheerien, J.P.; **J. G. McCrie,** O.B.E., M.B.; Miss A. Wetherell, S.R.N.

New members: Councillor Mrs. Olive Deer; W. E. Jones; Alderman E. A. Armstrong.

EAST ANGLIAN REGION

Reappointed: Mrs. Hester Adrian, J.P.; C. R. Caselton; P. F. Dennard; **J. V. Morris,** M.B.; Colonel J. D. Portway; Miss J. G. Thompson, S.R.N.; Alderman Mrs. Mary Whitmore.

New member: H. Payne, J.P.

Digitized by Google

NORTH-WEST METROPOLITAN REGION

Members reappointed: **A. C. Morson,** O.B.E., F.R.C.S.; Miss Vera Dart; **Horace Joules,** F.R.C.P.; **H. E. A. Boldero,** F.R.C.P.

New members: M. Hackett; Miss M. L. Hall, S.R.N.; Mrs. Blofield; Alderman Mrs. B. A. Beaumont, J.P.

NORTH-EAST METROPOLITAN REGION

Members reappointed: Alderman C. E. S. Blackmore; Captain H. Brierley, O.B.E., M.C.; **Somerville Hastings,** F.R.C.S., M.P.; Alderman S. F. Johnson, J.P.; E. T. Neathercoat, C.B.E., J.P.; C. S. B. Wentworth-Stanley; C. C. Carus-Wilson, M.C.

New member: Miss Rootham, S.R.N.

SOUTH-EAST METROPOLITAN REGION

Reappointed: Alderman R. H. Burslem, J.P.; Dame **Barrie Lambert,** D.B.E., M.B., J.P.; Alderman Rev. Harcourt Samuel; **J. R. H. Turton,** F.R.C.S.

New members: T. W. Stigger; **H. C. Edwards,** C.B.E., F.R.C.S. Two further appointments.

SOUTH-WEST METROPOLITAN REGION

Reappointed: **P. H. Mitchiner,** C.B., C.B.E., F.R.C.S.; J. A. Tulk, J.P.; **J. M. Wyatt,** F.R.C.S., F.R.C.O.G.

New members: W. H. Tooes; Alderman H. Regan, J.P.; Mrs. M. Ormerod; D. Jackman, M.B.E., J.P. One further appointment.

OXFORD REGION

Reappointed: Prof. **A. D. Gardner,** D.M.; Alderman Mrs. A. Jenkins, J.P.; Miss R. R. Jolliffe, S.R.N.; P. C. Raffety, J.P.; **J. S. I. Skottowe,** M.D.; A. J. B. Selwood.

New members: F. Etherington; Mrs. French.

SOUTH-WESTERN REGION

Reappointed: **A. L. Candler,** F.R.C.S.; **R. E. Hemphill,** M.D.; Alderman J. Milton, J.P.; Miss R. C. Shackles, S.R.N.; **Samuel McClements,** M.R.C.S.

New members: Councillor F. A. C. Riddick; C. Rew; The Very Rev. **Garfield Williams,** O.B.E., M.B.; **N. L. Capener,** F.R.C.S. One further appointment.

WELSH REGION

Reappointed: **R. D. Aiyar,** F.R.C.S.E.; **A. H. Coleman,** O.B.E., F.R.C.S.E.; H. G. Davies, M.R.C.S.; Richard Davies; Alderman Richard Gronow; Mrs. H. Evans, J.P.; Prof. E. A. Owen; Mrs. E. Owen, S.R.N.; Rev. B. Waldo-Lewis.

New members: Alderman E. Williams, J.P.; Eugene Cross.

BIRMINGHAM REGION

Reappointed: **Norman Duggan,** F.R.C.S.; Major Cyril Hotchkiss, J.P. Prof. **H. F. Humphreys,** O.B.E., M.C., M.B., M.D.S.; Sir **Leonard Parsons,** F.R.C.P., F.R.S.; **J. J. O'Reilly,** M.B.; Alderman W. T. Smith, J.P.

New members: G. V. Grimshaw. Three further appointments.

MANCHESTER REGION

Reappointed: **Walter Briggs,** M.B., J.P.; Miss L. G. Duff Grant, R.R.C.; Sir Thomas Tomlinson, J.P.; Councillor T. Hourigan; Major E. F. Pilkington, J.P.; Alderman Joseph Eastham, J.P.

New members: Alderman T. H. Adams, J.P.; Alderman S. T. Marron, J.P.; Prof. **W. I. C. Morris,** F.R.C.O.G.

LIVERPOOL REGION

Reappointed: **D. Brown,** M.B., J.P.; Miss M. Jones, O.B.E., R.R.C.; J. F. Mountford; **D. R. Owen,** F.R.C.S.E.; Alma Parkin, J.P.; Prof. **H. H. Stones,** M.D., M.D.S.; Alderman David Plinston, J.P.; Ernest Smethurst, J.P.

New member: W. Gibbs.

In England Now

A Running Commentary by Peripatetic Correspondents

"YOU are a famous pianist," Mr. Ralph Slater told five sleeping figures at the Princes Theatre on April 4, "and you are giving a recital. The piano is there in front of you—go on, play." The young woman, the young man, the two elderly men, and the unmistakeable professional man turned to at once and gave of their best, as Uckridge used to say. Hypnosis is always fascinating, and I had never seen five people under at a time before. The most striking thing was the way in which differences of personality survived in these automatons. The girl—she turned out later to be an almoner at one of our teaching hospitals—played her imaginary piano with feeling and delight, enjoying the pleasure she was getting and giving, and enthralled by her own success. One of the elderly gentlemen, who told us later he was a civil servant, kept his hands to himself and waggled his fingers up and down; the other one ranged the piano wildly and enthusiastically. He was a printer of music, of some eminence, and a beautiful subject for hypnotism, accepting every suggestion with gusto. He was probably playing Rachmaninoff's prelude. The professional man—he proved to be a dentist—appeared to play rather well. The young man (he worked in a bank) gave us a series of powerful chords. The same sorts of differences appeared at every stage. When told they were three-year-olds crying for their mother, the girl, the young man, and the music-printer played the part quite passionately, while the dentist and the civil servant could barely manage an inhibited whimper. When told they had all been drinking bumpers of neat whisky, the dentist moved carefully and with great dignity, the girl seemed to get a violent headache, the civil servant looked troubled; but the young man and the music-printer danced and sang without embarrassment: they saw no harm in being merry, but clearly the other three found it disgraceful. Mr. Slater, whose slow delivery nearly put the audience to sleep for other reasons in the course of a very long evening, is adept at inducing hypnosis: at one point he had about twenty people asleep at once. He kept his five chosen subjects asleep for well over an hour, and put them to sleep again with a clap of the hands after he had roused them. He showed us all the classical tricks, including some amusing examples of post-hypnotic suggestion. He passed a lighted match under a sleeper's hand, stood on the stomach of a subject lying rigid between two chairs, and took a few rather cruel liberties with human dignity. On the whole he was considerate, however, and certainly he was competent. It was interesting to note how he picked his cases: the tough young man was needed for the rigidity demonstration, the pretty girl to be made to kiss her favourite film star, the professional man and the civil servant—both reserved and dignified—for prestige, and the music-printer because he was an asset to any performance, awake or asleep. But is there much to be said for making unconscious people behave foolishly in public? They ask for it, of course: they were all volunteers; and there is not the least doubt that they were strangers to Mr. Slater and genuinely hypnotised. I think I would rather see rabbits come out of a hat.

* * *

I have found a superb use for medical circulars, though it will doubtless make the child psychologists shudder: a promise of these coloured brochures will induce my small sons to finish their breakfast quickly when all else fails. Distribution requires the sagacity of a Solomon, but from experience I consider one picture of *Atropa belladonna* is roughly equivalent to a picture of a skeleton, clothed apparently in strands of red string, plus the portrait of a sleeping beauty. Lately, alas, breakfasts have tended to be protracted, and the reason, I find, is vitamins. There has been a spate of literature about them, and little else, and coloured but picture-free pieces of shiny paper will not get one mouthful of food swallowed the quicker. My children must have pictures, even if only of a spastic colon, and until manufacturing chemists once more turn their artists

Digitized by Google

on to flowers, or men (external or internal), I shall have to revert to the psychologist's "couldn't-care-less" method of persuasion.

* * *

The president of the section of medicine of the Royal Society of Medicine has recently examined the value of the anamnesis, in an exposition judicious if perhaps a little lukewarm. I know at least one aspirant to consulting practice whose experience in an examination has made him an unqualified enthusiast of its application. Approaching his long case with the stereotyped inquiry "what do you complain of?" or possibly, if he was a stylist, "of what do you complain?" he received the welcome information "I burn my fingers whenever I smoke a cigarette."

Nobody should be penalised for good luck, but surely in such an instance Dame Fortune is over-generous. To avoid the overwhelming advantage derived from mere interrogation, I suggest the insertion of the following advertisement:

WANTED.—A sufferer from syringomyelia who is deaf and dumb, or is able to simulate these disabilities. Remuneration at the rate of 15*s*. a day with lunch and tea and the guarantee of an interesting experience.

* * *

I have noticed that small delinquents, sent to me from the police-court to be certified fit for caning, often wear rubber bands round the wrists or ankles. I asked one what they were for, and after some hedging he revealed that the bands are to secure the booty of a successful pocket-picking hidden under sleeve or trouser leg.

* * *

May I add two peripatetic memories to your memoir[1] of George Cockroft of Middleham? One, in the hard winter of 1940–41, is of a scene reminiscent of the "Flight into Egypt" of our Sunday-school books. A doctor, mounted on a horse, riding into the compound of the Darlington Memorial Hospital, with, behind him, on the pillion, a nurse holding, somewhat precariously, a baby sewn up in a blanket. With the roads impassable for a car, he had ridden ten miles into the hills, collected the intussusceptive baby, together with the nurse, and brought them as far as Richmond. Failing to find motor transport readily, he continued his ride into Darlington—perhaps in the spirit of mild perversity which had enabled him to overcome so many difficulties of rural practice. It is good to record that the infant made a complete recovery.

The other memory is of an afternoon spent with him in the spring of the year when Dante, in his brother-in-law Matt Peacock's charge, won the Derby; together we went round the old Castle of Middleham, reviving its history, and inspecting relics that Cockcroft had himself dug up. Among them was Warwick the Kingmaker's enema syringe, with its male and female parts, made of leather—the latter with a long tubular nozzle, the former a bag holding about two ounces of oil. To make the injection this was rolled up as one rolls a tooth-paste tube. Later there was tea—Yorkshire cheese-cake, with (tell it not in Gath or war-time) real Wensleydale cheese. After tea, round the stables with Matt Peacock, looking at the two-year-olds and finishing with Dante. "Put your arm round his neck, Mum, give him a kiss, and he'll win Derby." She did, and he did.

Wensleydale has a medical tradition which must be difficult to live up to. The Cockcroft practice was already established when John Fothergill, the famous Quaker physician of the 18th century, was born there; and George Cockcroft had several first editions of his works. But the tradition is certainly maintained. Quoting Saintsbury's dictum that: "unintelligent acquiescence in opinion is not only dangerous, it is immoral," Cockcroft would add that as this was true of literary criticism, how much more should it be true of medicine. Perhaps the most distinguished practitioner in Britain lives and works in Wensleydale, and he, I know, would agree that he is but *primus inter pares* with his fellows in following Fothergill's example of faithful and enlightened service to the community.

1. *Lancet*, March 17, p. 504.

Letters to the Editor

THE GENERAL PRACTITIONER

SIR,—May I congratulate you on your leading article of April 2? It is high time that something was done to improve the standing of the general practitioner, but we very often find that the reverse is happening.

Supernumerary hospital posts are shortly to cease. How, then, is the demobilised Service medical officer, who has been denied clinical responsibility and has therefore failed to maintain professional skill, to re-equip himself for active practice?

Dr. Plesch makes several proposals regarding medical education. I agree that much of the useless theoretical knowledge should be jettisoned, but it would surely be ridiculous to shorten the undergraduate training-period, as he suggests. Much of the general practitioner's work is concerned with the donation of philosophy to his patients; and to make a man capable of this—among many other things—we must give him as long a training as is feasible. There is no doubt, much as I dislike compulsion, that the standard of medical practice would improve greatly if one year in resident hospital posts was made obligatory prior to registration.

As things stand, many students, and even more responsible people, tend to have less and less respect for the "backbone of the profession." I am sure that if some of Dr. Plesch's proposals were adopted they would lower the general practitioner's status even more. More of the brighter men from the medical schools must be attracted into this great branch of medicine, in order to raise it again to its rightful place. It is regrettable that so many doctors slip into general practice as a last resort, and thus with little enthusiasm.

Farnborough, Hants JOHN S. TAYLOR.

SIR,—I read with interest your leader, and the letter of Dr. J. Plesch. I write as a general practitioner and I appreciate your sympathy over the burden of our work. Since I left the Army I have kept statistics. In the first three months of 1947 and 1948 I had an average of 3990 consultations and visits. This year it rose to 5188—an increase of 30%. By and large the people need us and we must see the matter through to better days.

I cannot agree to the principle of lowering the standard of the general practitioner. We have, over the past half-century, lost a lot of our responsibilities to the specialists: but new fields of medicine and new interests have arisen to take their place. Surely the standard of G.P. medicine should be raised and not lowered. This can be fostered by team-work, each doctor having his own bias. Of the colleges, the Royal College of Obstetricians and Gynæcologists is the only one which meets the needs of the G.P. by its diploma. It should be possible for G.P.s to study special subjects and get recognition of their efficiency in them, without reaching for the standards of the true specialist. There should be a D.C.H., a D.A., and a D.P.M. for G.P.s. I do not like examinations as such, and I realise their shortcomings, but if one can achieve something objective, it is an incentive to keep up with one's studies. The chaotic state of hospitals today is due to the fact that cases are referred to specialists which should never leave the G.P.'s consulting-room for another opinion. This is due in part to the strain of overwork, and the fear to accept responsibility on our part. This vicious spiral can only be stemmed by G.P.s standing firm. We must treat all we can on our own: and safeguard the hospitals as much as possible.

The home, with familiar faces and objects around, is the proper place in which to treat most of the sick. Hospitals can and do produce their own peculiar diseases, by over-investigation and their failure to deal with patients in a personal manner. Your pages have recently had some very revealing articles on the shortcomings of institutions.

We general practitioners are specialists: specialists in personal medicine. In general it may be said that the personal touch is a bigger weapon in the fight against disease than any single therapeutic agent or reassuring

Digitized by Google

X ray. The basis of the doctor-patient relationship is confidence. How is real confidence to be maintained if the G.P. is debased to an orderly directing his patients to the most appropriate specialist?

No-one realises more than I do the value of specialists: but there is too much specialism today. The more one specialises, the more one becomes a technician and the less a physician. Already the pathologist and the radiologist have ceased to be physicians, and there are more to follow.

Nor do I agree that research-workers are a race apart. It is obvious that certain types of research can only be done by the laboratory worker: but there is room in the vast field of medicine for research in every sphere, and this includes general practice. If a general practitioner has no special interest, he stands in danger of getting stale and out of touch with modern trends. His special interest keeps him alert—a jack of all trades, maybe, but a master of *one*.

Much more propaganda is needed in the medical schools on the attractions and possibilities which lie in general practice. Most students end up as G.P.s, but how many lectures do they get on general practice? They are filled with ambitions to follow the masters of physic and surgery and only as a last resort do they descend to general practice. Little do they realise what soul-satisfying work it can be. The only touch they have with the outside world is the caustic comment of the house-surgeon on the foolishness of G.P.s.

To conclude, I feel that the high standard of British medicine depends on a high standard in general practice. This can be abetted by the following measures:

(i) Team-work among G.P.s so that different aptitudes can be combined to avoid, as far as possible, recourse to specialists.

(ii) More teaching on general practice in the medical schools. Why not a chair in general practice?

(iii) The grim determination of G.P.s to see this crisis through: and to refuse to lower their standard of efficiency.

These are dark days: but it is only hard work which will put us through to the better times ahead.

Ibstock, Leicester. C. H. WATTS.

SIR,—As a general practitioner of the younger generation, I was particularly interested by your leading article of April 2.

The medical services in this country, as I see them, comprise a threefold structure, whose component parts are contributed respectively by hospitals and consultants, public-health medical officers, and general practitioners. No mention was made in your leader of the second of these, which surprised me, because collaboration with his public-health colleagues, in the field of child health for instance, is an important part of the general practitioner's work. The three components already referred to are complementary and must remain both integrated and well balanced, if the medical services are to work efficiently. This essential condition would no longer hold good were the status of any one of them to be lowered, either in professional ability or public regard, as undoubtedly would occur if the suggestions of Dr. Plesch regarding medical education were ever taken at all seriously.

Professor Ryle once gave an address at Cambridge, entitled The Physician as Naturalist, describing the doctor as a student of φυσις or nature, and his particular field of study the sick man in relation to the whole of his environment. The general practitioner has peculiar opportunities for assuming this rôle. For he is able to survey the whole field of medicine without bias, and it is his privilege to spend a great part of his time visiting the sick in their homes, thus acquiring first-hand knowledge of that most intimate part of their environment. In addition to this, however, the scope and responsibility of the general practitioner are continually increasing with every advance made in the specialists' fields. To appreciate this point it is only necessary to consider what extra demands on one's clinical judgment are made, for instance, by the advent of streptomycin in the treatment of tuberculous meningitis, by the increased indications for surgery in peptic ulcer, or by the discovery of the part played by the rhesus factor in maternity work. In the field of social medicine also, as its researches begin to bear practical fruit, the general practitioner is sure to have an important part to play on account of his special opportunities for access to the patient's environment.

It is my belief that general practice today, although marred for the time being by the gravest financial anxieties, holds out the promise of work of increasing interest and responsibility, and the prospect also of being able to maintain one's intellectual integrity, not necessarily an easy thing to do in a highly organised State service.

Oxford. G. A. BALLANCE.

BENADRYL IN PARKINSONISM

SIR,—Lest recent reports should be too discouraging, I should like to give my experience. After reading the article by Dr. Ryan and Dr. Spurway Wood, in your issue of Feb. 12, I prescribed 'Benadryl' 4 capsules a day for a patient, aged 52, who has been under my care for paralysis agitans for the last nine years. She had become practically helpless, could not move in bed, get up, bathe, dress, or feed herself without help. A few days later she telephoned that it had worked a miracle. She has to a very large extent lost her rigidity; her face and speech are now normal; she sleeps without discomfort, and can get up, bathe, and dress without help. The relaxation of her fingers allows her to use her knife and fork again, and even her typewriter.

The tremor persists, and there is little improvement in her gait, but she has regained her independence and takes a new interest in life.

London, N.W.1. E. A. GATES.

*** We have also had a letter from a parkinsonian of ten years' standing who says that he has had benadryl for six weeks and "the improvement is unbelievable."—ED. L.

CLINICAL ESTIMATION OF BASAL METABOLIC RATE

SIR,—In my letter of March 5 I avoided criticising Dr. Greene's first letter (Feb. 19) because I did not know whether he was speaking as a physician or as one who was technically responsible for the observations on metabolism by the staff of his clinic. Dr. Greene's second letter (March 26), however, repeats many of his previous errors, as well as introducing others, and indicates that he has not benefited by correspondence on the subject in THE LANCET.

1. Dr. Greene questions the meaning of "correspondence" and says that in my article I did not suggest that the R.P. index is to act as an "indicator," as I did in my letter of March 5. This omission was due, as I stated in my letter, to the shortness of my article. Furthermore, in applying the word "index" to my formula I presumed that this would be understood by readers to signify an indicator or guide. No correspondent except Dr. Greene has had any difficulty in comprehending this. There is therefore no question of a "reduced claim."

2. Dr. Greene has not repeated my work. His reference to charts implies that the pulse and respiration rates must have been counted after at least half an hour's rest. Is he sure that the rate (and/or amplitude) of respiration is the same with and without a face-appliance? We know that a face-appliance can alter the carbon-dioxide output.

3. Dr. Greene's criticism of my 5-minute rest period is valueless. As Dr. Robertson (Feb. 19) has pointed out, "in seeking to make an intelligent guess at the basal metabolism, by a formula in no way related to heat output, it is not essential to comply with standard heat-output conditions."

4. And now for a study of some of Dr. Greene's cases which he quotes. (*a*) In thyrotoxicosis a respiration-rate at rest of 7 per min. is unusual. It would be interesting to determine in this case the mean respiratory excursion, the minute-volume, and the ventilation equivalent. (*b*) Dr. Greene quotes a B.M.R. of + 56% and an R.P. index of 960. Since the diagnosis of thyrotoxicosis has been confirmed histologically, the diagnosis cannot be doubted. But Dr. Greene must also admit that it is very uncommon for a patient with severe thyrotoxicosis to have a pulse-rate of 60 and a respiration-rate of 16 per min., or of 80 and 12

Digitized by Google

respectively. (c) Next, the case with the B.M.R. of — 3 and R.P. index of 2700. This would represent a pulse-rate of 135 and a respiration-rate of 20, or say 90 and 30 respectively. It is surely even more uncommon that a normal person should have such rates. There certainly must be a cause for this unusual picture, but Dr. Greene found "nothing organically was amiss."

5. Dr. Greene accuses me of seeking to turn the diagram by Miss Lovell and Dr. Martin (Feb. 12) "into a piece of evidence in his favour . . . by changing his views about the lower limit of the normal R.P. index, which he formerly considered to be 1100 and now considers to be 900." I pointed out in my reply (March 5), that "this correction depends on what should be taken as the lower limits for pulse and respiration rates. The difference in the normal range between Miss Lovell and Dr. Martin's cases and mine could be due to the different duration of the rest applied before the investigation, as Dr. Robertson wisely suggests; they insisted on 30 min. rest, whereas I insist on only 5 min." I also refer to Dr. Jordan's letter (Feb. 26): "Dr. Bene claims a good correspondence of results in about two-thirds of cases; I submit that this claim is supported by the figures of Miss Lovell and Dr. Martin."

If Dr. Greene is not impressed by my assumption that something is wrong somewhere when, with (?) thyrotoxicosis and a B.M.R. of + 90, there is no tachycardia, then I can forgive him when he says "the proportion of cases in which a B.M.R. is helpful in the diagnosis is comparatively small." It is small because the determination of the B.M.R. is open to error except in the hands of an expert. The casual observer is less likely to make a mistake in counting the pulse and respiration after 5 minutes than in measuring oxygen consumption under basal conditions.

In rejecting the usefulness of the R.P. index because it is "at its best approximately correct in only two-thirds" of cases, and simultaneously stating that the proportion of cases in which the B.M.R. is helpful is comparatively small, Dr. Greene makes the biggest contradiction. He attaches to such a complicated method as gas analysis a comparatively small usefulness and yet demands that such a simple method as is the R.P. index should be an absolute indicator in the diagnosis of thyrotoxicosis. Or does Dr. Greene suggest that Read and Boothby elaborated their formulæ without presuming their practical usefulness? By publishing their formulæ they certainly did see their applicability without claiming for them more than I do for the R.P. index—that it is a very good and simple help in establishing a clinical diagnosis.

London, W.8. EUGENE BENE.

LIVER EXTRACTS

SIR,—The recent correspondence, stimulated by Dr. Wilkinson,[1] regarding the suitability of pharmaceutical livers for the preparation of liver extracts has raised a question which can neither be avoided nor criticised in the manner implied by Mr. Shaw in his letter of March 26.

The reply by the Minister of Health[2] to the question raised in Parliament on Feb. 24 may be satisfactory inasmuch as the safety of a patient is not impaired by the injection of an impotent extract, but clearly the recovery of the patient may well be impaired.

Immediately after the cessation of European hostilities, I had the opportunity of examining several manufacturers' methods of liver-extract preparation in Germany. The impression gained regarding the necessity for fresh liver in the preparation of such extracts clearly supported the contentions of Dr. Wilkinson. During the war years, the Germans, like ourselves, utilised livers unfit for human consumption. The more obviously affected parts of cirrhotic and other diseased livers were excised before use. Nevertheless, the Germans preferred fresh livers and regarded liver of poor quality as likely to produce extracts of impaired potency.

Normally, the collection of livers in Germany was carried out with extreme care, fresh ox and cow liver being used, or frozen ox livers imported from the Argentine and Uruguay.[3] It would appear that precautions were taken to avoid freezing livers in too great a quantity; for in such large masses the interior showed signs of decomposition, with a greenish discoloration on thawing which the Germans also associated with low-potency extracts.

I believe that it is not uncommon for British manufacturers to find that considerable variation exists in the clinical potency of individual batches as processed, even though precisely controlled chemical methods are used for the purification of the extract. It would appear, therefore, that the main source of variation is the original liver, and in view of the Germans' experience and practice, as well as the experiences cited by Dr. Wilkinson, the desirability of the use of fresh liver for the preparation of parenteral extracts cannot be too strongly emphasised.

Chorley Wood, Herts. J. B. M. COPPOCK.

SIR,—Your comment on Dr. William Murphy's letter (April 2) refers to "concentrated 'refined' extracts which are popular in the U.S.A., but which we are not allowed to import," and draws a distinction between them and the "purified" extracts prepared by the technique of Dakin and West and other similar methods. The implication of this statement is that there is available in America a special class of liver extracts that are more highly refined, concentrated, and potent than the best extracts manufactured in Britain. Such, however, is not the case. Equally refined and highly concentrated liver extracts are manufactured in this country and have been available for many years. The Dakin and West process to which you refer, or modifications of it, is simply one of the processes by which highly refined extracts are manufactured.

It has been the common practice in Britain to have each batch of liver extract tested clinically to ensure that it reaches an accepted standard of activity. The practice of clinical standardisation of each batch is less common in America. There it is the custom, on the basis of a clinical test, to assign to each new extract when it is first manufactured a certain potency designated in terms of "*U.S.P.* units," and it is assumed that all batches of extract prepared thereafter by the same method and by the same manufacturer will have the same potency. Such a presumption is unwarranted. Every manufacturer of liver extract is well aware that occasional batches may fail on clinical testing to show the required degree of activity and so have to be discarded.

Further and more precise confirmation of variability among American extracts has recently been forthcoming consequent upon the isolation of the crystalline anti-anæmic factor, vitamin B_{12}, and the development of microbiological methods for assessing quantitatively the amount of anti-anæmic factor present in purified liver extracts. Reference may be made to a paper by Rickes et al.[4] who reported that the vitamin-B_{12} content of seven commercial preparations of American liver extracts, all designated as 15 *U.S.P.* unit material (the highest designation that any American extract may bear), varied from 1·2 to 14 μg. per ml. No-one would now claim that extracts containing such widely divergent quantities of the common anti-anæmic principle could all be equally effective clinically.

The effectiveness of the crystalline anti-anæmic factor in the treatment of pernicious anæmia is well established. It has also been proved to be effective against the neurological complications and it produces remission of the lingual symptoms. Moreover, the substance has also been shown to be effective in the macrocytic anæmia of sprue and in the nutritional macrocytic anæmia of the tropics. The theory of multiple essential factors being present in injectable liver extracts becomes, therefore, extremely doubtful, and an active extract, be it "crude" or highly refined, acts by virtue of its content of the common principle, vitamin B_{12}. Nor is it too much to hope that, in the near future, the treatment of anæmias responding to liver therapy will be defined with considerable precision in terms of weight of anti-

1. Wilkinson, J. F. *Lancet*, Feb. 5, p. 239; *Ibid*, Feb. 12, p. 249; *Ibid*, Feb. 19, p. 291; *Ibid*, Feb. 26, p. 336.
2. *Ibid*, March 5, p. 420.
3. B.I.O.S. rep. no. 116; item no. 24; appendix 7(1). B.I.O.S. rep. no. 449; item no. 24; p. 22. B.I.O.S. rep. no. 766; items no. 22 and 24; p. 247. C.I.O.S. rep. no. 32–47; item no. 24; p. 105.
4. Rickes, E. L., Brink, N. G., et al. *Science*, 1948, **107**, 396.

Digitized by Google

anæmic factor required by the individual patient. It can be expected that liver extracts designated simply as crude, purified, concentrated, or refined, or carrying an arbitrary designation of potency expressed in a somewhat nebulous and doubtful unitage, will give place to preparations that contain a declared amount of the known active anti-anæmic factor.

Glaxo Laboratories Ltd., Greenford. H. M. WALKER.

MEDICAL TREATMENT ABROAD

SIR,—In your issue of March 26, which contains my previous letter, you report the Economic Secretary to the Treasury as saying that:

> "There was no question of refusing currency to anybody who could improve his chances of recovery as a result of going abroad. The Exchange Control Medical Advisory Committee did not question the medical facts as stated by the patient's doctor. They were not a group of bureaucrats but considered the cases sympathetically and liberally."

But the truth is that the committee *does* question the medical facts as stated by the patient's own doctor, and makes its decision on inadequate premises. The only men who can fairly judge the issue are the patient's doctor and the consulting chest physician who are on the spot. And it is impossible to give "sympathetic consideration" to shadows seen in an X-ray film.

Mr. Walter Elliot's letter of April 2, quoting extracts from Mr. Glenvil Hall's, does not, in my view, excuse the existence of this committee. The committee is redundant, since most patients who ask for currency are known to the chest physician of the area in which they live and make application to him. If he cannot be trusted not to recommend for currency those who would not increase their chances of recovery by going abroad, it does not appear that anyone else, in the absence of knowledge of the patient, can be trusted to come to a fair decision. No appeal tribunal set up and working as this one does can solve the problems involved without injustice to applicants.

B. G. EDELSTON
Chest Physician, South-East
Folkestone. Metropolitan Regional Hospital Board.

THE EOSINOPHIL CELL

SIR,—I was very pleased that Dr. Lendvai, in his letter of April 2, raised the subject of ovalocytosis in human beings.

Parallel with our studies on camel blood, we had a case of familial ovalocytosis in father and son, and in both these patients it was found that the proportion between ovalocytes and round cells was very even. The eosinophil cells in the peripheral blood contained

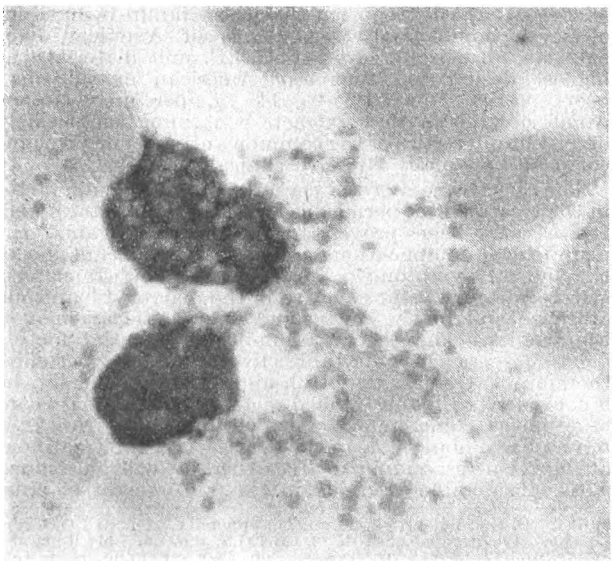


Fig. 1.

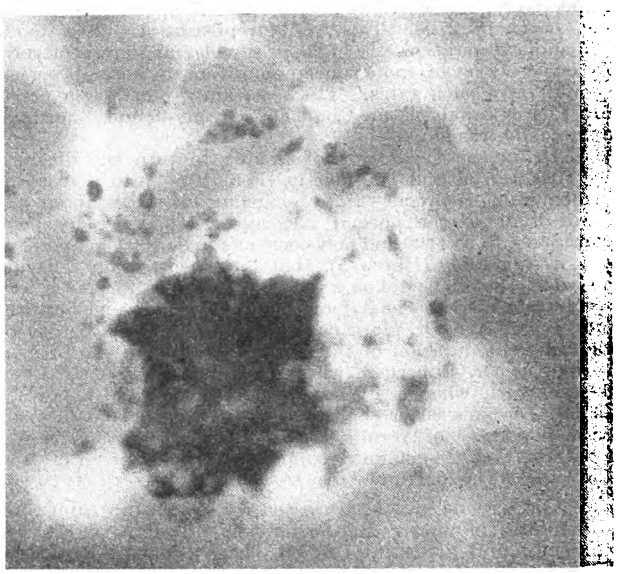


Fig. 2.

oval granules, as we had seen in the camel, and in the broken eosinophils, where the granules are more evident and can be classified, the proportion between round and oval granules was similar to the proportion between the round and oval cells, as shown by the accompanying photomicrographs. As we had been able to investigate only two patients we did not feel justified in being dogmatic about our findings; but as Dr. Lendvai raises the point I should like to take this opportunity of disclosing our observations, limited though they are. Further studies of camel spleen, which we hope to publish elsewhere, demonstrate clearly that in this organ there are numerous large cells full of oval granules, and the graduation in size of both cells and granules can be followed without difficulty.

Ancoats Hospital, Manchester. F. DURAN-JORDA.

ROAD ACCIDENTS

SIR,—*Cave canem*, or should it be *caveat canis*? Dr. Sandler (April 2) suggests a very high-pitched whistle to warn dogs of the approach of his vehicle. A simpler method is to bang with the hand on the outside of the driver's door. This usually makes dogs look up and run out of the way.

For those who are troubled by dogs when on foot, it is enough to bend down and pretend to pick up a stone: nearly all dogs slink away. If they do not, the pretence of throwing the imaginary stone should be adopted.

Henleaze, Bristol. HUGH R. E. WALLIS.

Parliament

Paying for our Social Services

IN introducing his Budget on April 6 Sir STAFFORD CRIPPS, Chancellor of the Exchequer, said that investment in the social services as a whole should be very little less than last year, with a slight decline in the total cost of housing activities, and an almost corresponding increase in capital investment on education, the health services, and water-supply. It would be impossible to reduce Government expenditure, and therefore taxation, so long as defence and the social services were provided on the present scale. When he heard people speaking of reducing taxation and at the same time saw the cost of social services rising rapidly, often in response to the demands of the same people, he wondered whether they appreciated to the full the old adage that one could not have one's cake and eat it.

Last year the people of this country enjoyed an unexampled national dividend in the form of a free National Health Service at the cost, for 9 months of its

Digitized by Google

duration, of £208 million. Next year for 12 months this service was estimated to cost £268 million. Such expenditure must be paid out of the national income of the community by taxation. If this was not done unflinchingly we should face inflation.

The reduction or elimination of the Budget surplus arose, he continued, primarily from the increase in Government expenditure on defence, food, and social services. The social services were a permanent and continuing obligation which automatically increased as those services inevitably developed. The more and better the services given, the more must be the cost. If, for instance, the 60,000 hospital beds at present closed for want of staff were brought into operation, as it was hoped they would be, another £15–20 million would be added to the cost of the health services. The cost of social insurances would increase in the same way. Nothing could stop that increase except cutting down of the social services, and he did not believe anyone was prepared to recommend that. They must therefore recognise the unpleasant fact that those services must be paid for by taxation, direct or indirect.

A great and highly desirable redistribution of wealth had already taken place over the last few years within our community. To a large extent that had resulted from the provision of the extended social services for the less well-to-do at the cost of the more well-to-do. That had been a purposeful policy most successfully carried through, but there was not much further immediate possibility of the redistribution of national income by way of taxation. For the future they must rely rather on the creation of more distributable wealth than upon the redistribution of the income which existed. Total taxation, local and national, was now more than 40% of the national income, and at that level the redistribution of income entailed in the payment for social services already fell to a considerable extent upon those who were also the recipients of those services. We must therefore moderate the speed of our advance in the extended application of the existing social services to our progressive ability to pay for them by an increase in our national income. Otherwise we should not be able to avoid entrenching to an intolerable extent on the liberty of spending by the private individual for his own purposes.

Looking at Government expenditure as a whole, the Chancellor said he had thought it advisable to issue a Treasury circular asking all departments to review again the expenditure which was likely to flow from the development of existing policies so that it could be kept within the bounds of what was considered feasible. In particular, he had emphasised that only in special cases —for example, major changes of policy—could any supplementary estimates in future be permitted.

Food subsidies had risen from £63 million in 1940–41 to £485 million at the present time, and it was estimated that, if the present prices were maintained and there was a very moderate increase in supplies, as was hoped there might be this year, the total subsidies payable would amount to no less than £568 million, all of which must be found by taxation on top of the other prospective increases already mentioned. That could not go on, Sir Stafford declared. We must call a halt or else we should find ourselves in the ridiculous position of having to refuse to import much-needed food because we could not afford to pay the subsidy out of our Budget. The Government therefore proposed to put an effective and firm limit on subsidies. If there was a further rise in cost it would have to be added to the price. He proposed that, as from early dates to be arranged by the Minister of Food, the following increases in prices to be charged retail should be made: Cheese, 4*d.* per lb.; meat, 4*d.* per lb.; margarine, 1*d.* per lb.; and butter, 2*d.* per lb. These changes would cause a rise in the cost-of-living figure on the all-items index of rather less than 2 points.

There was a curious idea abroad, Sir Stafford said, that as a result of last year he had a surplus. That money had all been used for disinflation. There was indeed, he continued, a good argument for imposing some special charge or tax in connexion with the health services, both to help to finance them and to bring home to people that they had to be paid for out of taxation. It might be argued that this might make people more economical in their use of the services. But he had come to the conclusion that we should await the outcome of another year before taking such action. He hoped there would be such economy in the use of the services as to make it unnecessary. We had chosen, he concluded, to have our benefits in the form of extended social services, which had brought the people increased comfort and easement of their conditions. We must face the consequences of that deliberate choice.

QUESTION TIME

Eradication of Bovine Tuberculosis

Mr. A. R. HURD asked the Minister of Agriculture if he had completed his consultations with the farming organisations and the veterinary profession on the arrangements to be made for the systematic eradication of bovine tuberculosis, and the establishment of clean areas; and when he would put such a scheme into operation.—Mr. TOM WILLIAMS replied: While discussions with the interests concerned show that there are no wide differences of view as to the main principles on which an area eradication plan should be based, a few difficult questions remain as regards the financial provision of such a plan. I hope, however, that these may be resolved in the near future. Meanwhile, substantial progress continues to be made under the voluntary tuberculosis (attested herds) scheme which now includes nearly a million and a half cattle.

Composition of National Flour

Dr. BARNETT STROSS asked the Minister of Food what amounts of vitamins A, B_1, and B_2, and calcium were available in wheaten bread; and what were the corresponding amounts in the pre-war white loaf.—Mr. JOHN STRACHEY replied: I assume that by "wheaten bread" the hon. Member means bread made from National flour of 85% extraction-level. There is no vitamin A in bread. The comparative figures for the vitamins B_1, B_2, and calcium of the national and pre-war white bread are as follows:

	National (mg. per oz.)	*White* (mg. per oz.)
Vitamin B_1 (Thiamin)	0·063	0·015
Vitamin B_2 (Riboflavin)	0·028	0·013
Calcium	31	3

Dr. STROSS asked the Minister what variation there had been in the rate of extraction of wheat in the preparation of flour during the past four years; and what was the type of reinforcement of flour now in use.—Mr. STRACHEY replied: During the past four years the rate of extraction of national flour has varied between 80% and 90%. The current rate of extraction is 85%. National flour is reinforced with calcium (creta preparata) at the rate of 14 oz. per 280 lb.

Medical Referees

Mr. GRANVILLE SHARP asked the Minister of Health what were the functions of part-time medical referees on the regional staff of his department.—Mr. ANEURIN BEVAN replied: The part-time medical referees examine insured persons on reference by the Ministry of National Insurance and advise on the question whether they are incapable of work. They also examine disabled persons referred by the Ministry of Labour and National Service in order to advise disablement resettlement officers on general questions under the Disabled Persons Acts, 1944.

Beds for the Tuberculous

Mr. SOMERVILLE HASTINGS asked the Minister how many fully staffed beds were available for the treatment of tuberculosis in England and Wales in 1945, 1946, and 1947.—Mr. BEVAN replied: The numbers of beds at the end of 1945, 1946, and 1947 respectively were approximately 27,340, 27,150, and 28,830.

Provision of Analgesia

Lady TWEEDSMUIR asked the Minister when he expected to receive the final recommendations of the Medical Research Council as to the latest types of analgesic drugs and apparatus suitable to be administered by midwives alone.—Mr. BEVAN replied: No forecast can yet be given. Although existing methods will no doubt be reviewed by the committee which has been set up, the question remitted to the Medical Research Council by the Working Party on Midwives was on the possibility of devising improved methods. This is a relatively long-term project involving the initiation and conduct of actual research work, and quick results are not to be expected

Digitized by Google

Obituary

GILBERT WILLIAM DE POULTON NICHOLSON

B.A., M.D. CAMB.

Professor Nicholson, who died on March 11, held the university chair of morbid anatomy at Guy's Hospital until his retirement in 1944.

Of his work as one of our greatest histopathologists, R. A. W. writes: "Nicholson's studies in pathological anatomy, especially the pathology of tumours, are remarkable not only for their accuracy and their beautiful illustrations—the product of his own hand—but for their profundity and philosophical flavour. His passion for careful examination and description, his scathing impatience with careless or superficial work and with ill-founded hypothesis, and his wide and sound knowledge of general biology as well as of human pathology, combined to make his writings classics. Their versatility and the amount of detailed factual information which they contain are astonishing. The general and special pathology of tumours, the structure and nature of teratomata, ovarian goitre, endometriosis, heterotrophic tissues, metaplasia—these are only some of the subjects dealt with in Nicholson's papers and many of them dealt with more authoritatively, more critically, and more presciently than by any previous writer. His work cannot be appreciated by the hasty superficial reader or by the utility-monger. It is the work of a great microscopist, scholar, and philosopher; and those who read and reread it will find it a storehouse of both information and wisdom. A collection of his papers reprinted in one volume would be a stimulus to pathologists both young and old, a great ornament to English pathological literature, and a fitting memorial to a too-little-appreciated scientist."

An old friend, R. D.-C., adds these personal lines: "Of Irish and German parentage Nicholson inherited many of the characteristics of both races, and his early education in the stilted and conventional atmosphere of Coburg was probably responsible for a habit of intolerance and a brusqueness of manner, which never quite left him and were apt to create an unfavourable first impression. But those who knew him well realised that he was really one of the kindest and most generous of men and the truest of friends. He loved children and understood them, and there must be many, now grown up, who cherish the memory of happy hours spent with him in their childhood. Outside his work he was fortunate in having hobbies which took him out of London into the pure air of the country. He was a great walker in his younger days and an ardent naturalist, and he was never happier than when rambling in the woods and fields in search of beetles, of which he amassed an enormous collection, and on which he was a noted authority. On these occasions he was the most delightful of companions and a fund of information on every branch of natural history.

"He cannot be said to have been a good teacher of undergraduates. Routine classes were always irksome to him, and a nervousness when confronted with an audience was a great handicap. For the same reason he was rarely seen at pathological meetings. But to anyone who was genuinely interested in his subject he would open his heart and give freely of his vast knowledge and experience, and those who were admitted to the intimacy of his sanctum at Guy's considered themselves fortunate indeed to have known and learnt from so great a master.

"From his early days at Jesus College Nicholson always retained a great affection for Cambridge and the fen country, and on his retirement he went to live there, almost under the shadow of his old college. Though his health was failing, his last five years were happy ones, and his final illness came suddenly and was short."

After taking his B.A. at Cambridge in 1899 Nicholson went to Guy's to complete his medical studies. In 1905 he graduated M.B. and he held house-appointments there until in 1907 he was awarded a Gull studentship. A period as an assistant in the research department of the Cancer Hospital followed till in 1913 he was appointed morbid histologist and director of the department of clinical microscopy at Guy's. Nine years later he became reader in morbid histology and in the following year demonstrator of normal histology. The title of professor was conferred on him in 1928, and in 1945 he was made professor emeritus in recognition of his services to the university and to morbid anatomy.

ARTHUR HEDLEY CLARENCE VISICK

M.B. LOND., F.R.C.S.

Arthur Visick, who died at the York County Hospital on April 4, was one of the leading surgeons in the North of England. He came from a long line of doctors, his father, grandfather, and greatgrandfather having been members of the profession. His sister, Mrs. Griffiths, is consulting surgeon to the New Sussex Hospital for Women and Children, Brighton.

He was born in Hampstead in 1898, and was educated at Epsom College and St. Bartholomew's Hospital, London, where he won an entrance scholarship in 1915. As a student he won many prizes and distinctions, including the Treasurer's anatomy prize, the Foster anatomy prize, the Willett operating surgical medal, the Walsham pathological prize, and the Brackenbury surgical scholarship.

[Yorkshire Evening Press

After house-appointments and a chief assistantship to the surgical unit at Barts, he obtained a Rockefeller scholarship and went to the U.S.A., where he held the appointment of assistant surgeon and instructor in orthopædic surgery in the University of Michigan. During his stay there he reorganised the methods of admission and of record-keeping. His main interest, however, was the surgery of the thyroid, in which he was an assistant to Peet.

On his return to England he went to York in 1928 and was appointed to the staff of the York County Hospital, and later, when it was opened in 1942, to the City General Hospital, York. He devoted his services to these two hospitals until his death at the early age of 51.

A. V., as he was affectionately called, was an outstanding surgeon. In his early days in York, his interest lay mainly in the surgery of the thyroid; but in later years, especially since 1941, he had devoted his energies to developing the technique of gastric surgery, which in his hands reached a high level; and his operative results were as good as any in the country. He gave himself unsparingly to his work on peptic ulcers, which received both national and international recognition; he was a Hunterian professor, and was awarded the Bishop Harman prize for 1948. He was not content with the operative work alone, but organised a very complete follow-up system; and in recent years it was rare that a week went by without a visit to his gastric clinic by a surgeon from somewhere in the British Isles or abroad, to study his technique and results. It always grieved him that physicians did not seem to be interested in the

Digitized by Google

possibilities of surgery for peptic ulcers. The very large number of his patients who attended the funeral service in York Minster on April 6 was perhaps a more telling testimony of his results than any of his published statistics—impressive as they are.

Arthur Visick was an appreciative and understanding colleague. He was never afraid to speak his mind, and had no use for careless or inefficient work; but he had a remarkable ability for attracting affection from all who worked with him, and from his patients. He was keenly interested in all aspects of hospital work, being chairman of the York County Hospital house-committee, and a member of the local hospital management committee.

Apart from surgery his interests were simple; he was fond of country pursuits, and his chief happiness lay in his life at home and in his family. He married Christine Ruegg in 1929, and they had one daughter and two sons.

C. N. P.

C. G.-W. writes: When Arthur Visick served as my chief assistant at St. Bartholomew's some thirty years ago, I realised that he was cut out for surgery. When the war brought me to York early in the war, I found he had become a well-known and highly respected surgeon and had acquired a reputation for gastric surgery. A Hunterian professorship gave him the opportunity to present before the Royal College of Surgeons a most careful statistical analysis of some 500 cases of gastrectomy with remarkable end-results. When I had to submit to this procedure, I placed myself with confidence in his hands, and splendidly he justified my confidence.

Our sympathy goes out to his wife and family, for he was essentially a happy family man. He lived for his family and his work. The remarkable gathering in the Minster at his funeral showed how much he was beloved by friends and patients; truly he was a lovable character. For the County Hospital and the people of York his loss will be difficult to repair.

Public Health

Mineral Oil in Food

THE Mineral Oil in Food Order, 1949, which came into force on April 9, prohibits the use of mineral oil as an ingredient of food manufactured for sale to the public. Announcing the Order, the Ministry of Food observes that prolonged and regular consumption of medicinal paraffin

"may lead to deposits of the oil in certain organs of the body. Deposits of medicinal paraffin would not, in so far as is known, be harmful in themselves, but the same cannot be said for other mineral oils, many of which are known to contain harmful substances. Moreover, too little is known about the fate of deposits of mineral oils, including medicinal paraffin, in such organs as the liver, for the medical profession to remain indifferent about them. The regular consumption of liquid paraffin has other unfortunate consequences. The paraffin, whether medicinal or not, dissolves vitamin A (and its precursor carotene) and vitamin D, and inhibits the assimilation of these essential vitamins by the digestive system. Experiments have shown that as much as 50% of vitamin A and carotene may be lost in this way when liquid paraffin is substituted for fat in the diets of laboratory animals. . . . In view of the harmful effects which might result from the indiscriminate use in this way of mineral oil, including medicinal paraffin, housewives are strongly urged not to purchase or to use these substances as substitutes for edible oils in home cooking."

The use of mineral oil in food was discussed in our issue of April 2 (p. 586). In a report on the incorporation of liquid paraffin in bread, to keep it fresh—a practice which has been tested at a Paris bakery—the Académie Nationale de Médecine [1] points out that the country is unable to produce the amount of paraffin required for the general adoption of the method, and that bread treated in this way would have a laxative effect.

1. *Bull. Acad. Méd. Paris*, 1949, **133**, 122.

News

University of London

The degree of D.SC. has been conferred on Dr. F. R. Selbie.

University of Edinburgh

On Monday, May 2, at 5 P.M., in the physiology lecture-theatre, University New Buildings, Teviot Place, Dr. Douglas Guthrie will give the first of a series of lectures on the Historical Approach to Medicine.

University of St. Andrews

The James Mackenzie Institute for Clinical Research has given over £15,000 to the university for the endowment of professorships in child health and in public health and social medicine.

Royal College of Surgeons of England

At a meeting of the council on April 7, with Lord Webb-Johnson, the president, in the chair, the Jacksonian prize for 1948 was awarded to H. L. M. Roualle (St. Bartholomew's Hospital) for his essay on malignant disease of the thyroid gland. A certificate of honourable mention and an honorarium was awarded to C. G. Rob (St. Thomas's Hospital) for his essay on the same subject.

The John Hunter medal and triennial prize were awarded to P. M. Daniel (Oxford) for his research on "the discovery of afferent nerves and muscle spindles in the external ocular muscles: also contributions to the discovery of shunt in the renal circulation."

The following were elected fellows of the college without examination: Mr. Arthur Woo (Hong Kong), Mr. R. J. Cann (Guy's Hospital), Prof. Robert Bradlaw (Newcastle), Prof. Thomas Yeates (Middlesex Hospital), Prof. D. E. Derry (Cairo), and Mr. A. B. Nutt (Sheffield).

Mr. P. H. Mitchiner was elected an examiner for the primary fellowship examination. Prof. Kurt Thoma (U.S.A.) was appointed Charles Tomes lecturer for 1949.

The fellowship of the faculty of anæsthetists was granted to Dr. G. F. V. Anson (New Zealand). The Begley prize for anatomy and physiology was awarded to W. H. McBay (King's College, London).

The following diplomas were granted jointly with the Royal College of Physicians:

D.P.H.—J. H. F. Norbury, Alexandrina M. M. Parker.

D.T.M. & H.—M. H. M. Abdulcader, A. Z. Abduttam, P. B. Adamson, Doreen M. Bottone, Wei-Hsien Chao, M. J. Colbourne, C. D. Desai, C. C. Draper, G. M. Edington, R. T. D. Emond, M. K. D. Hagopian, T. K. Howat, H. C. Jeffrey, V. V. Kalbian, S. F. Liu, M. F. McDowall, Megat Khas Bin Megat Omar, A. R. Mills, G. P. Mohanty, I. S. Mudie, E. J. D. Nariman, Muniswamappa Ramu, V. G. Rao, R. G. Rowberg, A. B. Roy, Emanuel Shirajian, George Skinner, A. J. W. Spitz, Carlos Suarez, C. K. M. Thacker, A. H. Wahba, A. A. Zaki.

D.O.M.S.—A. L. Alban, A. E. Barrett, G. T. Bedford, P. L. Blaxter, H. A. Bramwell, Berysz Brodkiewicz, A. N. Cameron, M. A. Carpenter, Hsi-Hua Chang, D. P. Choyce, L. N. Deshmukh, B. K. Dhir, G. C. Gulati, Florence I. Henry, A. P. K. Homayouni, P. L. Kiewe, Jack Levy, Kathleen M. Long, A. J. A. McCormick, F. E. McLaughlin, James McMillan, G. P. Mann, V. A. F. Martin, S. B. Mukhopadhaya, D. P. North, Abina T. O'Connor, I. W. Payne, T. J. G. Price, S. A. Qadeer, Toni J. Riegele, W. L. Robinson, C. M. Ruben, R. P. Sarda, M. D. Sengupta, W. A. M. Smith, I. B. Taylor, R. A. Trope, K. C. Wybar.

D.C.H.—Unity R. Allen, Manuel Anderson, Mary V. Ashton, G. N. Barsden, Aleida E. M. M. R. Bisschop, Margaret E. M. Blanden, J. H. Boydell, D. L. Bridgewater, J. F. Britto, A. D. Brown, Elizabeth R. M. Brown, Winifred C. M. Bulkeley, Sheila M. Burt, Alice M. Bush, C. D. Cassimos, Phoebe Charlton, H. M. T. Coles, Helen M. Connell, Dorothy J. Cooper, A. H. C. Couch, J. H. Coulson, D. H. Cownie, Margery N. Cummins, Joan P. D'Arcy, K. K. Datey, R. S. Dayal, Pauline M. Dean, Thomas Debney, Michael Elyan, A. D. Fair, Margaret L. Fallon, Marie A. Favard, Elspeth M. Frith, Betty B. Glansfield, Jean F. Gordon, Nathan Gordon, Joan M. Griffiths, Y. G. Gupte, G. J. H. L. Hall, A. G. Hesling, Alison Hunter, W. N. Ingham, S. E. M. Jarvis, H. R. Jolly, Mary P. L. Karney, Barbara M. Killick, Alison B. King, Catherine M. R. Kirkpatrick, A. A. Lewis, H. W. Macintyre, Ma Po Po, P. L. Masters, R. M. Mayon-White, Brenda M. Mead, Philip Micallef, Mok Hing Yiu, J. P. Mostyn, Putli Nanavatty, Jean S. Isbister, D. N. Patel, D. T. Pitt, J. N. Pohowalla, Diana Powell-Cotton, T. M. Pritchard, Helen Rennie, Catherine P. Schofield, L. G. Scott, Joan N. Scragg, Nivedita Sen, C. S. Shaw, Ka-Hee Siu, Louis Solomon, Ralph Spielsinger, Maude Stevenson, T. K. Sundaram, W. P. Sweetnam, Alexandra Tobert, D. Q. Trounce, Samuel Wayburne, J. A. Waycott, L. R. Whittaker, Edith H. Williams, Alice E. Wilmot, Margaret Wilson.

D.Phys. Med.—J. W. Byrne, C. W. Coplans, H. R. Davies, H. J. Glanville, Guy Savill.

D.M.R.-D.—Wlodzimierz Stachurko.

Almroth Wright Lectures

A course of six lectures on the bacterial cell will be held at the Wright-Fleming Institute, St. Mary's Hospital, London, W.2, on Tuesdays at 5 P.M., during the summer term. Further particulars will be found in our advertisement columns.

Digitized by Google

Royal College of Physicians of Ireland

On April 5 Lord Boyd-Orr was admitted to the honorary fellowship of the college. The oration was delivered by Dr. T. P. C. Kirkpatrick, registrar of the college. Afterwards Lord Boyd-Orr gave an address on Medicine in a Changing World.

The following, having passed the final examination in medicine, surgery, and midwifery of the conjoint board of Ireland have been admitted to the licentiateship :

J. G. Campbell, C. A. Cusack, J. J. Dollond, M. M. Marks, C. W. R. Murray, J. B. McCaffrey, W. J. McKeogh, Joan M. O'Connell, E. J. M. O'Connor, F. J. O'Hagan, Edward O'Rafferty, Julia O'Reilly, W. P. Timmon.

Royal Faculty of Physicians and Surgeons of Glasgow

The following have been admitted to the fellowship :

R. A. Blair, James Crorie, Sudhendu Kumar Ganguli, Ghulam-Hussein Velshi Keshani, Margaret M. O'Hare, C. M. Ross, I. A. Short, J. F. Smith, Mary D. Smith, R. A. Y. Stewart, F. H. Stone, W. O. G. Taylor, R. M. Thomson, J. D. Woods (qua physician); A. A. Bonar, Ewan Cameron, R. K. Dewar, John Ferrier, J. D. Fraser, T. B. Gardiner, Jayantilal Muljibhai Jalundhwala, George Johnstone, Mohammed Taqui Khaleeli, Douglas MacLeod, D. A. Macpherson, A. L. Morton, J. F. P. Mullins, Rameshchandra Manjanath Nadkarni, T. R. A. Richmond, Nagalingam Therugnana Sampanthan, Malcolm Shaw, Rabindra Narayan Sinha, George Smith, R. A. Tennent, J. K. Watt (qua surgeon).

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on March 26, with Sir William Gilliatt, the president, in the chair, the following were elected to the fellowship :

Doris C. Bates, R. B. Charlton, K. M. K. Duff, M. D. A. Evans, J. D. S. Flew, Barton Gilbert, J. W. Johnstone, W. I. C. Morris, Margaret M. Nolan, H. L. Sheehan, D. F. Standing, C. K. Vartan, William Waddell, W. W. Wilson, R. G. Worcester.

Harold Renton was elected to the membership.

A prize for an essay on the Physiology or Management of the Third Stage of Labour was divided between Dr. Jean Burton-Brown of Oxford and Dr. David Fletcher Shaw of Manchester.

Seminological Centre

The address of the Family Planning Association's seminological centre is now 64, Sloane Street, London, S.W.1. Facilities include a laboratory for the diagnosis of early pregnancy, and the results of tests will normally be available within 24 hours.

Congress of Catholic Doctors

The fourth International Medical Congress of Catholic Doctors will be held in Rome from Sept. 24 to 30. Further particulars may be had from Dr. W. J. O'Donovan, hon. secretary of the Guild of St. Luke, SS. Cosmas & Damian, 130, Harley Street, London, W.1.

Hospital Honours its Staff

On April 1 Sir Ronald Matthews, formerly chairman of the board of governors, opened the Ernest Finch medical library at the Sheffield Royal Infirmary. The library was first begun in 1946 with money subscribed by colleagues and former students on Professor Finch's retirement. Sir Ronald later unveiled a plaque renaming the dermatological department the Rupert Hallam Department of Dermatology. Neither Professor Finch nor Dr. Hallam were able to attend the ceremony, but Sir Ronald read letters which they had sent.

British Association

The annual meeting of this association will be held this year in Newcastle-on-Tyne from Aug. 31 to Sept. 7 under the presidency of Sir John Russell, F.R.S. The programme of the section of physiology includes discussions on adolescent nutrition, relations of brain to mind, microbial digestion in the alimentary tract, folic acid and anæmia, and a presidential address by Prof. R. A. Peters, F.R.S., on The Cell. Further information may be had from the secretary of the association, Burlington House, London, W.1.

British Hospitals Association

As a sequel to the nationalisation of the voluntary hospitals, this association, which includes the Central Bureau of Hospital Information, was voluntarily wound up on April 1, and Mr. E. F. G. Whinney, of Messrs. Whinney, Smith and Whinney, 4B, Frederick's Place, Old Jewry, London, E.C.2, was appointed liquidator. Until stocks have been exhausted, copies of the Central Bureau memoranda and of the *Hospitals Year Book* can be obtained from him. Mr. J. P. Wetenhall, secretary of the association, is chairman of the League of Hospital Friends, whose formation we announced last week.

Diary of the Week

APRIL 17 TO 23

Tuesday, 19th

SOCIETY FOR THE STUDY OF ADDICTION
4 P.M. (11, Chandos Street, W.1.) Dr. R. D. Newton: Alcoholism as a Neurotic Symptom.

Wednesday, 20th

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Mr. Joseph Minton: Occupational Eye Diseases and Injuries. (First of two lectures.)

ROYAL MICROSCOPICAL SOCIETY
5.30 P.M. (B.M.A. House, Tavistock Square, W.C.1.) Prof. J. Gough, Mr. J. E. Wentworth: Use of Thin Sections of Entire Organs in Morbid Anatomical Studies.

Friday, 22nd

BRITISH ORTHOPÆDIC ASSOCIATION
9.30 A.M. (University of Nottingham.) Opening of spring meeting.

Appointments

BARLING, G. M., M.B., B.SC. Birm.: ophthalmic surgeon, Peterborough area.
DUNKLEY, E. W., M.B. Lond., D.A., D.C.H., D.P.M.: asst. physician, department of psychological medicine, University College Hospital, London.
GEORGE, J. T. A., M.B. Birm., D.P.H.: M.O.H., Coseley, Staffs.
* KIMBELL, N. K. B., M.B. N.Z., M.R.C.O.G.: specialist obstetrician, Peterborough area.
NAPIER, F. J., M.B., D.P.M.: medical superintendent, Hellesdon Hospital, Norfolk.
RICE, H. M., M.D. Lond.: pathologist in charge of laboratory, Nottingham General Hospital.
ROYCE, G. B., M.B., B.SC. Leeds: chest physician, Peterborough area.
WILLIAMS, G. O., PH.D.Lond., M.R.C.S.: H.M. inspector of factories.
* Amended notice.

Births, Marriages, and Deaths

BIRTHS

BANKS.—On April 2, at Bangor, North Wales, the wife of Dr. P. J. Banks—a son.
BENNETT.—On March 27, at Singapore, the wife of Dr. Vincent Bennett—a son.
GRAHAM.—On April 1, in London, the wife of Dr. I. C. A. Graham—a daughter.
HYNES.—On March 30, at Godmanchester, the wife of Dr. John Hynes—a daughter.
McIVER.—On April 1, in London, the wife of Dr. Cecil McIver—a daughter.
MAREŠ.—On April 1, in London, the wife of Dr. Andrej Mareš—a son.
PHILLIPPS.—On March 31, the wife of Dr. W. H. Phillipps—a daughter.
REID.—On April 2, the wife of Dr. R. K. Reid—twin sons.

MARRIAGES

NUNAN—REYNOLDS.—On March 30, in London, William Nunan, M.D., to Marjorie Reynolds.
YOUNG—SMITH.—On April 2, in London, Robin Bryce Young, M.B., to Pamela Helen Isabel Smith.

DEATHS

GOW.—On April 3, at Dundee, Peter Fleming Gow, D.S.O., M.A., M.B. St. And., F.R.C.S.E., F.R.C.O.G., lieut.-colonel, I.M.S. retd.
HALL.—On April 7, at Hove, Donald George Hall, M.A., M.D. Camb., F.R.C.P., aged 72.
MILESTONE.—On April 4, at Croydon, Evelyn Stone Milestone, M.D. Brux., aged 85.
STANGER-LEATHES.—On April 4, Hugh Ellis Stanger-Leathes, M.R.C.S., D.T.M. & H., colonel, I.M.S. retd.
VISICK.—On April 4, at York, Arthur Hedley Clarence Visick, M.B. Lond., F.R.C.S., aged 51.
WINTER.—On March 31, at Taunton, Herbert Gregory Winter, C.B.E., M.C., brigadier, A.M.S. retd.

CORRIGENDUM: *Long-acting preparation of testosterone.*—The description of the manufacture of this preparation, given by Professor Carlinfanti and his colleagues in our issue of March 19 (p. 479), should read as follows:

To a solution of 1 g. of crystalline testosterone (melting-point 154·5°C) in 10 ml. of 96% ethyl alcohol is slowly added, with constant stirring, 20 ml. of an aqueous suspension of aluminium phosphate 7 mg. per ml. The mixture of small testosterone crystals and aluminium-phosphate particles is allowed to sediment, and the supernatant fluid is decanted off. The residue is made up to 40 ml. with saline solution. In the case of soluble antigens, there is no doubt that the aluminium-phosphate gel adsorbs the proteins employed. In the case of a suspension of crystalline testosterone, we may be dealing with an adsorption effect, for adsorption by crystals is not unknown; but it is possible that aluminium phosphate, promoting fibrous encapsulation, makes the hormone leak out slowly through the capsule wall. Certainly aluminium phosphate acts as a stabiliser of the suspension.

Digitized by Google

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

REORIENTATIONS IN NEUROLOGY*

Sir CHARLES SYMONDS
K.B.E., C.B., D.M. Oxfd, F.R.C.P.
PHYSICIAN FOR NERVOUS DISEASES, GUY'S HOSPITAL; PHYSICIAN TO THE NATIONAL HOSPITAL, QUEEN SQUARE, LONDON

THE traveller in the world of medicine often loses his way, and this is not surprising, for it is a world largely unexplored. There are maps, it is true, of a kind, with areas here and there as full of detail as a guide to London, but in the intervening spaces, mysterious and boundless, the wanderer may see so much that is strange and exciting that it is easy enough for him to become a sightseer instead of an explorer. This, I fear, is what happens to many of us clinicians, and the more experience we have the greater the temptation. Like Ulysses we feel that:

> "... all experience is an arch
> Where through gleams the untravelled world
> Whose margin fades forever and forever"

as we move. The gleam is tempting, but the true explorer must at times shut himself in his tent, unroll the map, and pinpoint his stages, or his journeying will avail nothing for those who follow after.

This, you may guess, is self-admonition. I should enjoy telling you stories, like Sir John Mandeville, of unicorns and two-headed men. Instead I shall try to find some bearings in a world which does not correspond very well with the maps with which I started. Of the printed guides the clinical textbook is, I suppose, the worst. When I was about to enter the wards I was advised by one of my most revered teachers to continue with the study of anatomy, physiology, and pathology, and apply what I learned to my own clinical observations before allowing myself to be prejudiced by the textbooks of medicine and surgery. This was good counsel.

For the neurologist anatomical charts have not altered much in the last quarter of a century, but the shape of physiology and pathology has changed and is ever changing. As for clinical observation, the eye seeth that which it comes prepared to see. A constellation of symptoms and signs which needs no telescope may pass unseen for ages until someone with inspired vision points it out. The syndrome of coronary thrombosis, unknown when some of us began our studies, is a good example. There was a time when the correlation of symptoms and signs with visible lesions offered a fine field to the explorer, but the localisation of the lesion has now become largely a matter of routine. The outstanding problems are those of pathology, and among these the most fascinating and elusive is that of the selective lesion. Why does the virus of poliomyelitis attack only motor cells? Why does lead poisoning hit the long extensors of wrist and fingers, leaving as a rule other muscles intact? Why is it that the Argyll Robertson pupil is so rarely due to any other cause that we can be almost certain of neurosyphilis? This is the kind of question that provokes us daily.

MYASTHENIA GRAVIS

Myasthenia gravis is perhaps the best understood example of the selective lesion. We know that it is due to a failure of the normal function of acetylcholine as transmitter of the impulse from nerve to muscle. There is still doubt about the exact cause of this failure. It may be due to failure of synthesis of acetylcholine, to local excess of cholinesterase, or to some toxic agent, like curare, which raises the threshold for acetylcholine at the end-plates. Whatever it is, the lesion is biochemical, invisible, and, in the earlier stages of the disease, reversible. The selective character of the disease does not end with its affinity for neuromuscular junctions. It may be only some of these that are affected. Often in the early stages the ocular and facial muscles are alone involved. This selective incidence on certain muscles is one of the mysteries of myasthenia gravis, but it is also to be observed in other diseases—for example, lead palsy. Can it be that there is differentiation of physicochemical structure even between one group of neuromuscular units and another, and corresponding differences between the structure of causal agents?

FAMILIAL PERIODIC PARALYSIS

Familial periodic paralysis is another example of a selective biochemical lesion. In persons with this disease anything which lowers the serum-potassium below a certain level will cause paralysis, and within paralysis there is again selection in that the muscles of the limbs and trunk are affected and those of the eyes, face, and throat spared, the distribution of weakness being opposite to that usually seen in the early stages of myasthenia gravis. The attacks can be cut short, and in many cases prevented, by giving the patient large doses of potassium citrate by mouth. I mention familial periodic paralysis because it is another example of a biochemical lesion which is invisible and reversible, and because it introduces the inherited factor, presumably an inborn error of metabolism. In persons who have not inherited this defect the serum-potassium may be artificially lowered without effect to levels which cause paralysis in those afflicted by the disease.

PORPHYRIA

This leads to the consideration of porphyria, another rare disease, which appears to be due to an inherited error of metabolism, and in which flaccid paralysis may occur, its distribution being like that of familial periodic paralysis. These patients, though generally healthy, have periodic episodes in which abdominal pain and distension, with constipation, delirium, and paralysis, often occur in this sequence and are associated with the excretion of porphyrins in the urine and fæces. There are few good descriptions of the paralysis, but the pattern in some cases is striking. Abbott and Evans (1946) describe a case with flaccid weakness first involving the proximal muscles of the upper extremities, especially the extensors, and next those of the forearm. The muscles of the pelvic girdle and thigh were affected, but less severely. The tendon-jerks in the upper limbs and the knee-jerks were lost, the ankle-jerks preserved.

I have recently seen a patient with this disease under the care of Dr. Denis Brinton in whom the neurological signs were exactly those which I have just described. After the illness had been diagnosed it was discovered that one of the patient's sisters had died of an obscure illness with symptoms suggestive in retrospect of porphyria, and of five surviving relatives examined three were excreting excessive quantities of porphyrins, though without clinical symptoms.

To study this disease one should, it appears, go to Sweden, where in certain country districts there are many afflicted families; Waldenström (1939) collected 143 cases, with neurological symptoms in nearly half. The paralysis, as he describes it, conforms with that which I have related, and Waldenström refers to it as of the Landry type. This leads me on again to ask what is meant by Landry's paralysis.

LANDRY'S PARALYSIS

Landry (1859) described, as a single group, cases of acute flaccid paralysis which may, for all we can tell, have included examples of poliomyelitis, polyneuritis, or even diffuse myelitis, but in the course of years our concept of Landry's disease has narrowed.

James Collier (1937) from his own experience emphasised prodromal symptoms in Landry's disease: malaise,

* An address given to the Manchester Medical Society on Feb. 2, 1949.

Digitized by Google

headache, lassitude, insomnia, anorexia, constipation, dyspepsia, or diarrhœa. He considered the disease to be a motor polyneuritis or at any rate indistinguishable from this. This is as far as he went in print, but in his own mind he believed that there was one clinical syndrome distinguishable from all the others for which privately he reserved the term Landry's disease. He thought it extremely rare, and characterised by a very rapid progressive and massive flaccid paralysis, without loss of sphincter control and without sensory symptoms, in a patient whose mind was perfectly clear and whose cranial-nerve functions were unaffected. He rang me up one afternoon when I had a full list of appointments to take me to see a case of Landry's paralysis at St. George's. I told him I could not go, I had patients to see; but he said characteristically that patients could be put off, but that I had probably never seen a case of Landry's disease in my life. I think he was right, and since that day I had seen only two others, until in 1947 at the Johns Hopkins Hospital Dr. A. M. Harvey not only showed me a third case but also demonstrated its pathology.

A woman, aged 34, with carcinoma of the cervix, had developed symptoms of uræmia, symptoms of the kind recognised by Collier as the precursors of Landry's paralysis. On admission to hospital her blood-urea level was 81 mg. per 100 ml., and, to anticipate, necropsy showed both ureters to be obstructed by growth, with consequent renal failure.

During the two weeks she had spent in hospital her symptoms had improved until about six hours before I saw her, when she complained of weakness in her legs, and from that moment she developed a progressive flaccid paralysis of limbs and trunk, which was complete at the time of examination except for the diaphragm, which was moving feebly. All the tendon-jerks and the abdominal and plantar reflexes were absent. There was no impairment of sensory function. The functions of the cranial nerves were normal; she was clear in mind and could speak and swallow. She had asked for the bedpan half an hour before I saw her and she had passed water normally. She died, in spite of artificial respiration, within forty-eight hours of the onset of her paralysis.

This was the typical picture of Landry's paralysis as I had been taught by Collier, but for Dr. Harvey it was something else. He had already had an electrocardiogram taken, which showed the changes characteristic of potassium poisoning, and the chemical report, which arrived later, gave her serum-potassium as twice the normal figure.

This remarkable clinical picture arising from a high serum-potassium in renal disease was first clearly described by Finch et al. (1946), and I have no doubt that it must explain some cases which have been called Landry's paralysis without any understanding of the pathology. Again we have an example of the biochemical lesion unsuspected because we did not know where or how to look for it. It is now easy to understand the failure of the neuropathologist to find the lesion in the spinal cord, for it belongs to the group of invisible lesions, probably at the distal end of the neuromuscular unit.

Now, the invisible biochemical lesion is of the kind that should theoretically, under certain conditions, be reversible, and this has proved to be true of episodes of paralysis in some of these cases. Gowers (1886) observed this in a single case of Landry's paralysis, and his comment is remarkable for its prescience. We must remember that in those days everyone thought in terms of inflammatory pathology. Gowers remarks of his case: "The symptoms passed away with a rapidity that seems incompatible with an ordinary inflammation of the cord," and he goes on to say:

> "Curare abolishes the function of the termination of the lower motor path—i.e., of the nerve-endings in the muscles. It may be that in this (Landry's) disease some toxic influence impairs in an analogous manner the function of the termination of the upper segment, paralyses the ramification in which, as we have seen, the pyramidal fibres must end in the grey matter and by which they are connected with the lower segment."

Gowers was almost certainly right when he suspected a biochemical lesion in his case of Landry's paralysis, and, having gone so far in his imagination, it is not surprising that he should have thought of a toxin like curare, whose action was well known in his day. What is most remarkable is his notion that a similar toxic action might affect a synapse in the central nervous system.

TRANSMISSION OF NERVOUS IMPULSE

It appears certain now that the acetylcholine-cholinesterase mechanism is the only means of transmission of nervous impulse to muscle, and one of the questions of great moment for the clinician is whether transmission at the synapse in the central nervous system is effected by a similar chemical mechanism. If so, he should be prepared to look for diseases representing a biochemical lesion of the acetylcholine-cholinesterase complex at this level. This question is still unsettled. The evidence for cholinergic transmission within the central nervous system was reviewed by Feldberg (1945), who considers it in some instances as good as, or better than, that available for the transmission by acetylcholine from motor nerves to motor end-plates. It is almost entirely derived from experiments on animals. There is, however, no doubt that acetylcholine and cholinesterase are present in considerable quantities in the central nervous system of man, and that under favourable conditions human brain can synthesise acetylcholine in vitro.

Finally there is the evidence provided by Grob et al. (1947), who gave di-isopropylfluorophosphate (D.F.P.) to volunteers. The only known action of D.F.P. on the nervous system is through its anticholinesterase effect. These workers found that the daily intramuscular injection of D.F.P. to normal people, in addition to producing the expected peripheral effects, caused excessive dreaming, insomnia, "jitteriness," restlessness, increased tension, emotional lability, and, in some cases, visual hallucinations. This led to an investigation of the electroencephalogram (E.E.G.), and it was found that, after the daily intramuscular injection of 1·5 mg. of D.F.P. for three or four days, in 17 out of 23 people striking alterations occurred in the form of increased amplitude and frequency, with the occasional appearance of high-voltage slow waves of the kind seen in epilepsy. In all 17 people the intravenous injection of 1·2 mg. of atropine restored the E.E.G. to normal within a few minutes.

This effect is consistent with the observation that atropine will diminish or abolish the effects on the E.E.G. produced by local application of acetylcholine to the cortex in animals. The observations of Grob et al. (1947) thus suggest not only that cortical activity may depend to some extent on cholinergic activity but also that D.F.P. has a selective action in enhancing this activity. This may be because the central nervous system is more permeable by D.F.P. than are other parts of the body, but one may also ask whether there may be more than one kind of cholinesterase, and whether the selective action of drugs, toxins, or deficiencies may be related to their effect on particular acetylcholine-cholinesterase systems.

Is it possible that the illness now known as endogenous depression may depend on some analogous biochemical disorder? It is an illness which may begin suddenly and last for a very long time, with spontaneous complete recovery, and, as we now know, can be reversed by crude stimulation of the brain with the electric current. It may be precipitated by physical happenings—fatigue or intoxication—in susceptible persons. The factor of heredity is of undoubted importance. May we have here an example of an inborn error of metabolism, yet

Digitized by Google

to be discovered, in certain respects comparable with that which is responsible for the symptoms of porphyria?

I have spoken of the biochemical lesion as if it were generally invisible and reversible, but this is untrue. What is probably true is that the less it is visible the more likely it is to be reversible, and the examples I have chosen on the peripheral motor side have been of the invisible reversible kind. In myasthenia gravis, curare poisoning, and botulism we have examples of a biochemical lesion directly interfering with neuromuscular transmission. In certain other diseases known to be due to disorders of metabolism there is impairment of conduction in peripheral or central neurones, sooner or later associated with visible lesions. We know nothing about the way in which these lesions are produced, and only a little about the relation between cause and effect. What we do know, however, is interesting, for we find that certain clinical patterns of disease, depending on the localisation of the lesions, are pretty constantly related to particular biochemical disturbances.

SUBACUTE COMBINED DEGENERATION OF THE CORD

Subacute combined degeneration of the cord, for example, is usually diagnosed with the greatest ease. The elderly patient comes complaining of paræsthesiæ in the legs and perhaps a little in the hands together with heaviness in the lower limbs. We find absent knee and ankle jerks and extensor plantar responses, with impairment of postural and vibration sense in the legs. We note a smooth tongue and lemon-yellow pallor, and our conclusions are that the test-meal will show a histamine-fast achlorhydria, and the blood a macrocytic anæmia, and that the blood picture can be restored to normal, and the lesions in the central nervous system can be arrested or improved, by the intramuscular injection of minute amounts of vitamin B_{12} (Berk et al. 1948). This is no mean advance in the charting of unknown territory, for the disease itself was unrecognised until Risien Russell, Batten, and Collier (1900) put it on the map.

Three aspects of this disease deserve special consideration: (1) the specific nutritional defect which is its cause; (2) the selective distribution of the lesions, involving posterior and lateral columns of the cord, and very occasionally the optic nerves; and (3) the reversibility of the lesion in the early stages. For there is no doubt that the extensor plantar response can become flexor, and vibration and postural sense return, with effective treatment.

OTHER NUTRITIONAL NEUROPATHIES

Subacute combined degeneration of the cord is the only one of the nutritional neuropathies so well understood, and therefore so easily treated. The others, of which we have had so large and tragic an experience among prisoners-of-war in the Far East, are easily enough classified according to their clinical patterns, but the precise nature of the deficiency remains uncertain. There were so many things lacking in the diet that it has been impossible to identify separate causes. There is nevertheless matter for thought provided by the clinical symptoms in these cases.

There seem to have been at least four distinct neurological syndromes: Wernicke's encephalitis; polyneuritis; retrobulbar neuritis and spinal ataxia, so often associated that they may be regarded as constituting one syndrome; and the much rarer spastic paraplegia. Each of these syndromes appears to have had a peak incidence at different times after the beginning of captivity and starvation. Only a small percentage of men, all apparently suffering from the same nutritional deficiency, were affected; and, apart from Wernicke's encephalitis with its usually fatal issue, the symptoms of each syndrome, having developed rather suddenly, remained stationary. There are the bare facts which provoke many questions to which there is no answer. One of the most intriguing is that of selective incidence. As Denny-Brown (1947) remarks:

> "Whatever the actual mechanism of deficiency or neutralisation of specific essential food factors resulting in the appearance of these various neurological . . . disorders, there nevertheless remains the fundamental question of localisation of effect. Whereas the material here presented gives little indication that the defective agents are known vitamins, it clearly indicates that the resulting disorders are highly specific. It is difficult to account for such localisation except by the postulation of some specific unknown metabolic factor or enzyme essential for the adequate performance of each susceptible function."

Experimental diets lacking specific vitamins or food factors have produced selective nervous lesions of various kinds in animals, the neuritis of pigeons lacking vitamin B_1 being the classical example. The studies of Swank and Adams (1948) on the production of ataxia in swine by means of a deficiency either of pyridoxine (vitamin B_6) or pantothenic acid have revealed specific lesions of peripheral nerves, posterior roots, posterior columns of the spinal cord, and sensory ganglia. These are examples only of what is now being discovered about the selective action of deficiencies.

ANTI-VITAMINS

The subject is, however, much more complicated than this, for it is clear that deficiency disease may be due not to the absence of a particular vitamin in the diet but to the presence in it, in excess, of a particular anti-vitamin. This has been proved to be the cause of the so-called Chastek disease observed (Green et al. 1942) in foxes bred for their fur in captivity and fed on raw fish. The symptoms are loss of appetite followed by ataxia, convulsions, and paralysis, and the lesions in the central nervous system have much the same character and distribution as those of Wernicke's encephalitis in man. It has been shown that the addition of an adequate amount of the uncooked fish to an otherwise balanced diet will produce this disease, but that if to this there is again added a sufficient quantity of vitamin B_1, the disease is prevented. There is in fact an antagonism between something in the fish and vitamin B_1, such that a known quantity of fish will inactivate a known amount of the vitamin.

HEPATOLENTICULAR DEGENERATION

Returning to the subject of nervous disease in man I must mention hepatolenticular degeneration as another outstanding example of a selective lesion of the nervous system associated with metabolic disorder. In this disease, which is familial, there are degeneration of the basal ganglia and cirrhosis of the liver, and Uzman and Denny-Brown (1948) have been the first to demonstrate in an early case, without evidence of liver dysfunction, the continuous and abnormal presence of amino-acids in the urine. This observation has since been repeated, not only in patients with the disease but also in unaffected members of their families. What this means we do not know, but it of course suggests the possibility of an inborn error of metabolism as the cause of both hepatic and lenticular damage. The discovery is comparable in some respects with that of porphyrins in the urine, not only of the patient with paralysis but also of his apparently healthy relatives.

DISSEMINATED SCLEROSIS

This leads me on to speculate about the nature of disseminated sclerosis, an exercise which, however aimless it appears, should be practised daily by all neurologists who wish to preserve their spiritual health. There are two questions I would put to you. First, what is the explanation of the extraordinarily rapid and complete

Digitized by Google

recovery observed in some of the episodes of this disease? Complete unilateral blindness, for example, with restoration of normal visual acuity in six weeks, or recovery from a complete motor and sensory paraplegia in two or three months without so much as an extensor plantar response remaining. Can this be explained except in terms of a biochemical lesion—i.e., an interruption of conduction due to the temporary breakdown of an enzyme system? The experiments of Hurst (1942) are of interest in this connexion. He injected monkeys with sodium azide, which inhibits intracellular oxidation systems, and found that repeated small doses produced a clinical picture comprising blindness, cerebellar ataxia, and weakness and rigidity of the limbs. The pathological lesion was necrosis of the white matter or, in slighter cases, partial demyelination, with especial incidence on the optic nerves and tracts. Assuming that demyelination must be mediated by enzymatic processes and must ultimately be explained on a biochemical basis, he propounds the question whether it arises directly from a specific poisoning of a particular enzyme system, or whether during a period of anoxia—histotoxic or otherwise—the cellular enzyme systems as a whole are thrown out of balance. For the neurologist it is tempting to believe that the first hypothesis is correct, and that there may even be particular enzyme systems in certain areas or tracts of white matter. This, if true, would explain, for example, the selective action of sodium azide on optic nerves and tracts.

My second question is: what is the explanation of the familial cases of disseminated sclerosis? Every neurologist has his own collection of these, and has possibly begun, as I did, sceptical of their identity with disseminated sclerosis because of their rarity, only to be convinced by his own observations that they could be nothing else. One possible explanation is that the disease might be due to an inherited biochemical disorder, as a rule clinically latent but revealed under certain conditions. It is conceivable that the significance of the familial cases of disseminated sclerosis may be all-important, and that we may find the disease related to an inborn error of metabolism when we know where and how to look for the clues.

INTERACTION OF DEFICIENCIES AND INFECTIONS

Having regard to the fact that bacterial toxins and neurotropic viruses, on one hand, and nutritional deficiencies, on the other, may each be highly selective in their effects on neural function and structure, it is not unreasonable to suppose that there might be interaction between them, either coöperation or antagonism. Bodian (1948) has reported an observation which may be of great importance in this connexion. He produced pyridoxine (vitamin B_6) deficiency in a rhesus monkey by the administration of the specific anti-vitamin desoxypyridoxine, and the animal developed poliomyelitis, as proved by clinical symptoms, histological examination, and transmission to other animals. This rhesus monkey was in contact with others which had been inoculated with the virus and therefore might be considered to be exposed to the infection, but the rhesus monkey is never known to contract poliomyelitis in this way, nor can it be infected by the mouth, being in these respects unlike the chimpanzee. Following up this observation, Bodian found it possible to infect the rhesus monkey with a single dose of the virus by mouth if previously treated with desoxypyridoxine, control animals being immune. Thus it seems pretty certain that a vitamin-B_6 deficiency in the rhesus monkey deprives the animal of its natural immunity to the virus when given by the mouth. This opens the way to speculation about interactions between specific vitamin deficiencies and susceptibility to virus or bacterial infection which are, to say the least, attractive.

ENVOI

I began this essay with the notion that I would start with an excursion into the biochemical field and then try the path of physics. There is just as much of interest in one direction as in the other, but I have taken up my time. I am aware that I have not lived up to the true explorer's standard. I have offered you no charts, only some scattered ideas about what we might look for in the gaps between known landmarks. For this I offer the time-honoured excuse of the clinician, never so elegantly phrased as by Sir Thomas Browne in his preface to the Vulgar Errors:

> "Some consideration we hope from the course of our profession . . . which . . . doth . . . much interrupt the office of our pens in their well-intended transmissions. Therefore surely in this work attempts will exceed performances, it being composed by snatches of time, as medical vacations and the fruitless importunity of uroscopy would permit us. And therefore also perhaps it hath not found that regular and constant style, those infallible experiments and those assured determinations, which the subject sometime requireth, and might be expected from others whose quiet doors and unmolested hours afford no such distractions."

REFERENCES

Abbott, K. H., Evans, H. S. (1946) *Bull. Los Angeles neurol. Soc.* **11**, 20.
Berk, L., Denny-Brown, D., Finland, M., Castle, W. B. (1948). *New Engl. J. Med.* **239**, 328.
Bodian, D. (1948) *Amer. J. Hyg.* **48**, 87.
Collier, J. (1937) Textbook of the Practice of Medicine. Ed. F. W. Price. London.
Denny-Brown, D. (1947) *Medicine, Baltimore*, **26**, 41.
Feldberg, W. (1945) *Physiol. Rev.* **25**, 596.
Finch, C. A., Sawyer, C. G., Flynn, J. M. (1946) *Amer. J. Med.* **1**, 337.
Gowers, W. R. (1886) A Manual of Diseases of the Nervous System. London; vol. I, p. 278.
Green, R. G., Evans, C. A., Carlson, W. E., Swale, F. S. (1942) *J. Amer. vet. med. Ass.* **100**, 394.
Grob, D., Harvey, A. M., Langworthy, O. R., Lilienthal, J. L. (1947) *Bull. Johns Hopk. Hosp.* **81**, 257.
Hurst, E. W. (1942) *Aust. J. exp. Biol. med. Sci.* **20**, 297.
Landry, J. B. O. (1859) *Gaz. hebd. Méd.* **6**, 472.
Russell, J. S. R., Batten, F. E., Collier, J. (1900) *Brain*, **23**, 39.
Swank, R. L., Adams, R. D. (1948) *J. Neuropath. exp. Neurol.* **7**, 274.
Uzman, L., Denny-Brown, D. (1948) *Amer. J. med. Sci.* **215**, 599.
Waldenström, J. (1939) *Acta psychiat. neurol.* **14**, 375.

EFFECT OF DIETHYLSTILBŒSTROL ON URINARY EXCRETION OF PREGNANEDIOL AND ENDOGENOUS ŒSTROGEN DURING PREGNANCY

I. F. SOMMERVILLE
M.B., Ph.D. Edin.
RESEARCH ASSISTANT, DEPARTMENT OF BIOCHEMISTRY

G. F. MARRIAN
D.Sc. Lond., F.R.I.C., F.R.S.
PROFESSOR OF CHEMISTRY IN RELATION TO MEDICINE

B. E. CLAYTON
M.B. Edin.
RESEARCH ASSISTANT, CLINICAL ENDOCRINOLOGY RESEARCH UNIT (M.R.C.)

UNIVERSITY OF EDINBURGH

THE proposal of Smith et al. (1946) to give diethylstilbœstrol by mouth as a prophylactic to pregnant women with histories of repeated accidents in pregnancy has attracted widespread interest, particularly in connexion with the high fœtal mortality associated with maternal diabetes. This proposal is based on the suppositions that many accidents of late pregnancy are referable to a deficiency in the secretion of progesterone and other sex steroids by the placenta, and that the secretion of these steroids can be stimulated with diethylstilbœstrol. The second of these suppositions is based on the interesting theories concerning the interdependence of œstrogen and progesterone metabolism, developed by the Smiths in a long series of papers published from 1931 onwards and recently reviewed (Smith and Smith 1948).

The Smiths believe (1) that the œstrogenic hormone (œstradiol⇌œstrone) is converted in the body not only

Digitized by Google

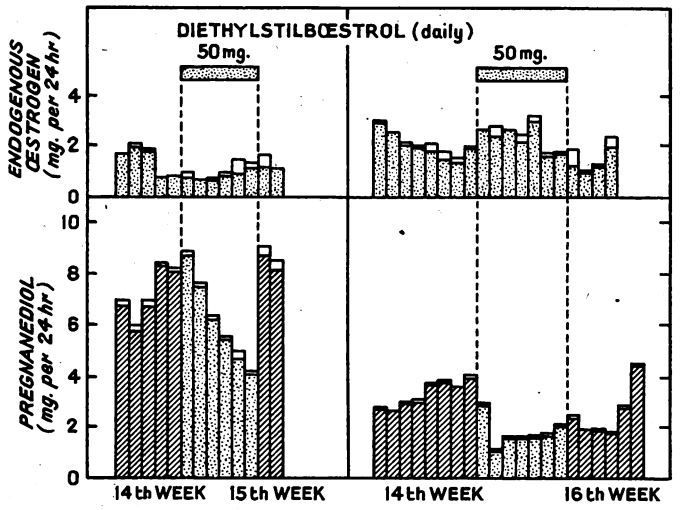


Fig. 1—Effect of diethylstilbœstrol on excretion of pregnanediol and endogenous œstrogen in a normal pregnant woman.

Fig. 2—Effect of diethylstilbœstrol on excretion of pregnanediol and endogenous œstrogen in a diabetic pregnant woman (case 1).

into œstriol but also into certain œstrogenically inactive oxidation products, which, however, have yet to be isolated and described; (2) that progesterone depresses the formation of these "œstrogen inactivation products" by facilitating the metabolism of œstradiol and œstrone by the alternative pathway to œstriol, and conversely that the formation of the inactivation products is enhanced when there is a deficient secretion of progesterone; and (3) that the œstrogen inactivation products play an important physiological rôle as stimulators of the secretion of progesterone and other "sex steroids."

These views led Smith et al. (1944) to suggest that massive doses of the œstrogenic hormone during mid-pregnancy might forestall an incipient premature deficiency in the secretion of progesterone and œstrogen from the placenta by raising the concentration in the body of these œstrogen inactivation products.

Later Smith et al. (1946) suggested that the artificial œstrogen, diethylstilbœstrol, might be more effective in stimulating the placental secretion of steroids, and they tried to test this suggestion by estimating the urinary pregnanediol excretion of a pregnant diabetic woman during intermittent treatment with this œstrogen. The results seemed to show conclusively that the excretion of pregnanediol had been increased by the diethylstilbœstrol,* and it was concluded that this increase was the result of a greater placental secretion of progesterone.

More recently some doubt on their findings has been cast by Davis and Fugo (1947), who claimed that the excretion of pregnanediol by non-diabetic women in early pregnancy was unchanged by treatment with diethylstilbœstrol. This claim calls for some comment. The published data show that no pronounced and progressive rise in the excretion of pregnanediol, like that observed by Smith et al. (1946), resulted from the treatment; but, since the pregnanediol excretion levels before treatment with the œstrogen were not established with certainty, the statement that the pregnanediol excretion was unchanged hardly seems justifiable. In any case, as Smith and Smith (1948) pointed out, the doses of diethylstilbœstrol used by Davis and Fugo were greatly in excess of those used by themselves; hence the two sets of experiments are hardly comparable.

We report here the results of a reinvestigation of the effect of diethylstilbœstrol on the urinary excretion of pregnanediol during pregnancy. Since the Smiths' theories imply that diethylstilbœstrol stimulates the secretion of œstrogen as well as of progesterone by the placenta, the urinary excretion of endogenous œstrogen has also been studied in these experiments.

METHODS

Daily 24-hour specimens of urine were collected in containers cooled with "dry ice" from all the cases studied. In most instances the completeness of the collection of urine was checked by determining the creatinine content by the method of Folin (1914). All determinations were carried out in duplicate on aliquot portions of the 24-hour specimens of urine.

Urinary pregnanediol was determined by the method of Sommerville et al. (1948).

Total urinary endogenous œstrogen (œstradiol + œstrone + œstriol) was determined by the method of Stevenson and Marrian (1947) using the Kober colour reaction, which is unaffected by the presence of diethylstilbœstrol in the urine. This method, though not so reliable as could be desired, is sufficiently accurate to detect any pronounced changes in the excretion of endogenous œstrogen.

RESULTS

One non-diabetic pregnant woman and three diabetic pregnant women were studied. The essential clinical points of the diabetics, for which we are indebted to Prof. D. M. Dunlop, were as follows:

Case	*Age (yr.)*	*Duration of diabetes*	*History of previous pregnancies*
1	30	Since childhood	—
2	30	2 years	Intra-uterine death 3 days antepartum
3	30	11 years	(i) Intra-uterine death 5 days antepartum (ii) Miscarriage at 19th week

Doses of diethylstilbœstrol greater than, less than, and the same as, those recommended by Smith et al. (1946) were given by mouth intermittently. Smith et al. recommended a dosage of 30 mg. daily at the beginning of the 16th week of pregnancy, increasing by 5 mg. a day at weekly intervals to the 35th week.

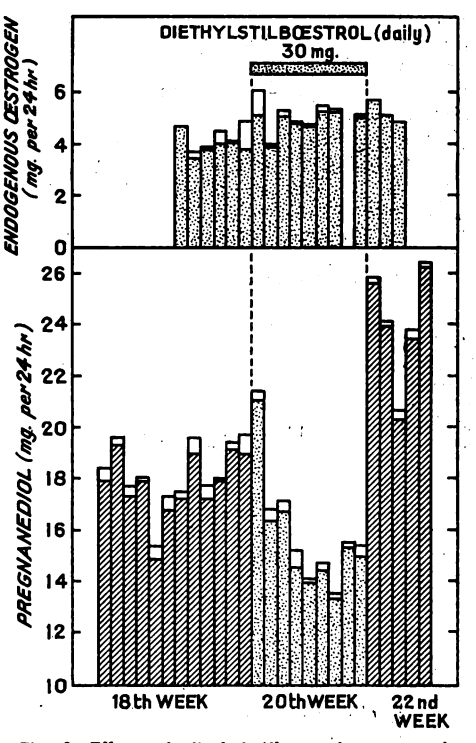


Fig. 3—Effect of diethylstilbœstrol on excretion of pregnanediol and endogenous œstrogen in a diabetic pregnant woman (case 2).

Details of the diethylstilbœstrol dosages and of the effects on the excretion of pregnanediol and endogenous œstrogen are shown in figs. 1–5,† from which it will be seen that the effect of diethylstilbœstrol on the urinary excretion of pregnanediol is unequivocal. In every instance

* Dr. O. W. Smith has privately informed one of us (G. F. M.) that she has obtained similar results with other pregnant diabetic women treated with diethylstilbœstrol.

† The values obtained in the duplicate determination of pregnanediol and œstrogen are shown by the double lines at the tops of the columns in each figure.

Digitized by Google

the giving of diethylstilbœstrol caused a sharp fall in the excretion of pregnanediol, whereas after withdrawal of the œstrogen the excretion rose either immediately or after a short delay.

The figures for the excretion of total endogenous œstrogen are unfortunately less clear-cut owing possibly to the known unreliability of the method of estimating œstrogen. It can be safely stated, however, that in these experiments the giving of diethylstilbœstrol caused no gross change in the excretion of total endogenous œstrogen.

DISCUSSION

The discrepancy between the results reported by Smith et al. (1946) and those reported here may possibly be due to the different methods used for the estimation of pregnanediol. The method of Sommerville et al. (1948), used in the present work, gives satisfactorily accurate and reproducible results when about 2 mg. of pregnanediol is excreted per 24 hours, and there is good reason to believe that it is reasonably specific for pregnanediol and *allo*pregnanediol. There can be little doubt, therefore, that the reduction in pregnanediol excretion following treatment with diethylstilbœstrol reported here was genuine.

Smith et al., on the other hand, used the original Venning (1937, 1938) method, which, it is now known, is not highly specific for pregnanediol. In this method sodium pregnanediol glucuronidate is extracted from the urine and weighed after "purification," the purity of the final product being checked by determining its melting-point. Unfortunately, however, the melting-point of sodium pregnanediol glucuronidate is unsatisfactory as a criterion of its purity. The compound decomposes at its melting-point, and this decomposition point may be affected to a relatively small extent by the presence of considerable amounts of other related substances. In actual fact Strickler et al. (1943), Mason and Kepler (1945), and Marrian and Gough (1946) have shown that the "purified" sodium pregnanediol glucuronidate fraction prepared from human urine by the Venning method may contain considerable amounts of the sodium glucuronidates of substances other than pregnanediol.

In view of these facts, the apparent rise in pregnanediol excretion following the administration of diethylstilbœstrol reported by Smith et al. (1946) may well have been due to the excretion of substances related to, but not identical with, sodium pregnanediol glucuronidate. In this connexion it should be pointed out that Dodgson and Williams (1948) have demonstrated the presence of a glucuronide of diethylstilbœstrol in human urine after the administration of diethylstilbœstrol by mouth. The possibility cannot be dismissed, therefore, that the results of Smith et al. were affected by the contamination of the sodium pregnanediol glucuronidate isolated by sodium diethylstilbœstrol glucuronidate.

Knowledge of the metabolism of progesterone is as yet so incomplete that it should not be assumed that changes in the excretion of pregnanediol in the urine necessarily reflect changes in the secretion of endogenous progesterone.

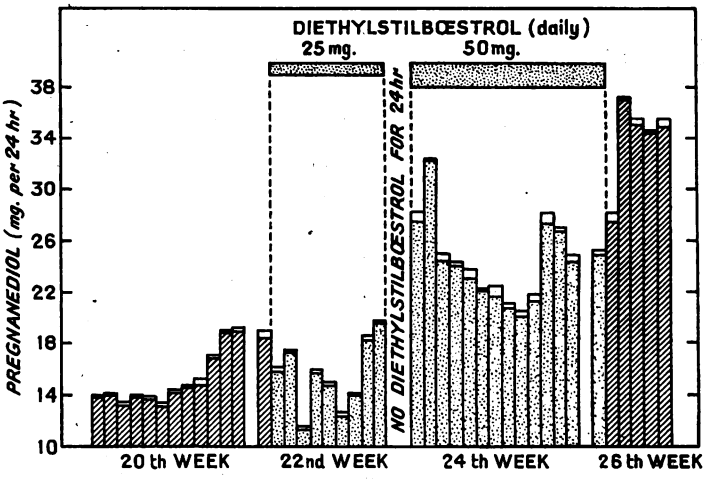


Fig. 5—Effect of diethylstilbœstrol on excretion of pregnanediol in a normal pregnant woman.

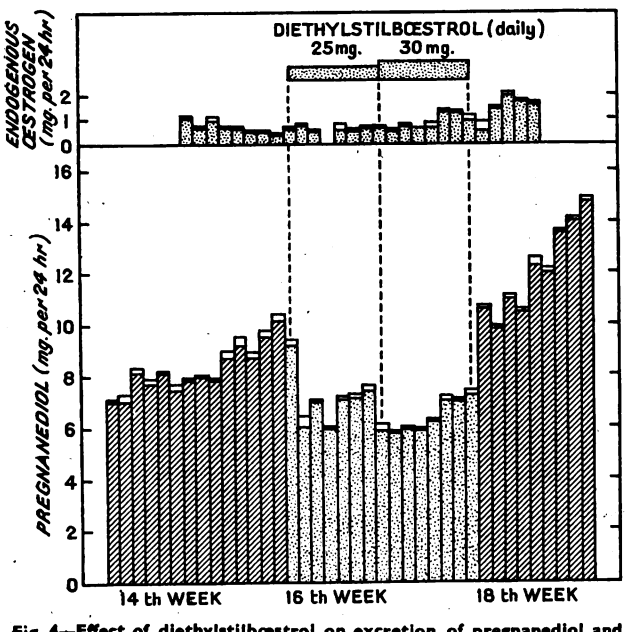


Fig. 4—Effect of diethylstilbœstrol on excretion of pregnanediol and endogenous œstrogen in a diabetic pregnant woman (case 3).

SUMMARY

The administration of diethylstilbœstrol by mouth to diabetic and normal pregnant women causes a sharp fall in the urinary excretion of pregnanediol. Withdrawal of the diethylstilbœstrol results in a rise in pregnanediol excretion, either immediately or after a short delay. These results differ from those reported by Smith et al. (1946).

The administration of diethylstilbœstrol causes no gross change in the excretion of endogenous œstrogen in diabetic and normal pregnant women.

We are indebted to the Medical Research Council for a personal grant to one of us (I. F. S.) and for a grant (to G. F. M.) out of which part of the expenses of this work was defrayed. We are also greatly indebted to Prof. D. M. Dunlop, Prof. R. J. Kellar, Dr. G. D. Matthew, and Dr. J. A. L. Gilbert for advice and coöperation; to Messrs. W. L. Aikman and H. A. F. Blair for technical assistance; and to Dr. Olive W. Smith, of the Fearing Research Laboratory, Boston, Mass., for so generously providing one of us (G. F. M.) with the opportunity of discussing with her the present results and those of her own investigations. This investigation was undertaken at the request of the committee of management of the Clinical Endocrinology Research Unit (Medical Research Council) in the University of Edinburgh.

REFERENCES

Davis, M. E., Fugo, N. W. (1947) *Proc. Soc. exp. Biol., N.Y.* **65**, 283; **66**, 39.
Dodgson, K. S., Williams, R. T. (1948) *Nature, Lond.* **161**, 604.
Folin, O. (1914) *J. biol. Chem.* **17**, 469.
Marrian, G. F., Gough N. (1946) *Biochem. J.* **40**, 376.
Mason, H. L., Kepler, E. J. (1945) *J. biol. Chem.* **161**, 235.
Smith, G. V., Smith, O. W. (1948) *Physiol. Rev.* **28**, 1.
Smith, O. W., Smith, G. V., Hurwitz, D. (1944) *Amer. J. med. Sci.* **208**, 25.
— — — (1946) *Amer. J. Obstet. Gynec.* **51**, 411.

Continued at foot of next page

Digitized by Google

IDIOPATHIC RENAL ACIDOSIS IN AN INFANT WITH EXCESSIVE LOSS OF BICARBONATE IN THE URINE

THOMAS STAPLETON
M.A., B.M. Oxfd, M.R.C.P., D.C.H.

From the Department of Child Health in the University of Sheffield

CASES of acidosis probably due to disturbances of renal function but occurring in the absence of demonstrable nephritis have been noted by several workers (Butler et al. 1936, Hartmann 1939, Peterman 1945, Payne 1948, Albright et al. 1940, Baines et al. 1945).

The case is reported here of an infant with chronic vomiting and failure to gain weight in whom a renal disorder was demonstrated and who subsequently recovered after the protracted administration of alkali by mouth. The kidney appeared to be unable to conserve bicarbonate when the plasma-bicarbonate level was low.

CASE-RECORD

The child was born on April 20, 1947, weighing 7 lb. 2 oz. Apart from possible slight constipation during the early months she was perfectly well until the age of $5^1/_2$ months. From that time until she was admitted to the hospital at the age of 10 months she was observed by various clinicians in the outpatient department because of chronic vomiting, up to five times a day and usually three times a day; she was very constipated, passing small hard motions only once or twice a week. At the age of 5 months she weighed 14 lb. 10 oz., and at the age of 10 months 13 lb. 6 oz. Throughout that time she was offered an adequate diet.

At the age of 10 months it was apparent that, though there had been some difficulty with the feeding, there must be some underlying organic disease, and so she was admitted for observation. The only abnormal physical signs were some loss of skin elasticity and the presence of hard fæces in the descending colon. Shortly after admission, at the age of $10^1/_2$ months, she became more ill, became dehydrated, with sunken eyes, and developed deep respirations. She remained constipated and she continued to vomit several times a day. For about ten days at that time she was febrile and had transient enlargement of the liver.

TREATMENT

On March 20 an intravenous infusion was begun; and it was observed that when she was given *M*/6 lactate 100 ml. in the intravenous fluid she improved clinically out of all proportion to the quantity of the fluid, an improvement which had not followed the administration of fresh blood, plasma, or physiological saline solution. The lactate was given because of the clinical evidence of acidosis—the deep respirations. So she was given *M*/6 sodium racemic lactate 180 ml. daily by mouth in six divided doses, and the vomiting became less. The infusion was stopped on March 29.

From March 22 to March 26, while on the intravenous infusion, the infant was given 'Sulphamezathine' 0·25 g. six-hourly. From March 21 to April 12 she was given penicillin 30,000 units three-hourly.

After three weeks the lactate therapy was stopped, and in thirty-six hours the child was again very ill and vomiting. She was then given lactate 360 ml. daily by mouth and within twelve hours her condition was greatly improved.

The biochemical changes in the blood and urine were observed after the infusion was discontinued and are shown in table I. The plasma-bicarbonate level was very low and the plasma-chloride level showed a marked rise. Throughout that time the freshly voided urine was constantly alkaline to litmus. Unfortunately, we have no record of the reaction of the urine before treatment was begun.

In view of the previous observations of Albright et al. (1940), Butler et al. (1936), and Payne (1948), a sodium-citrate mixture containing citric acid 60 g. and sodium citrate 100 g. in 1000 ml. of water was substituted for the sodium lactate. The child was given sodium citrate 6 g. daily in six divided doses, each dose being diluted to 45 ml. with water. This was a higher effective dosage of alkali, because the lactate which had been given was the racemic mixture, and there is evidence that the D-form is utilised to a less extent than the L-form (Hartmann et al. 1938). After two days on this higher effective dosage the plasma bicarbonate rose to the lower limit of normal. It was then found that the urine contained excessive quantities of bicarbonate, though the plasma bicarbonate was at the lower level of normal. When the citrate was stopped three days later, there was an immediate fall in the plasma bicarbonate, with a slow fall in urinary bicarbonate, loss of weight, and vomiting. There was an improvement shortly after the citrate was again given. These findings are recorded in table II and the accompanying figure.

On May 29, at the age of 13 months, the child was febrile and reluctant to take her feeds. Her urine contained about 20 leucocytes per high-power field, some of them being in clumps. She had developed a urinary infection. She was given a five-day course of sulphamezathine 0·5 g. six-hourly; her fever settled in thirty-six hours, and the urine cleared in three days.

On July 19, at the age of 15 months, after nine weeks, the citrate mixture was discontinued. The child weighed at that time 15 lb. $12^3/_4$ oz. She remained well without alkali therapy. Her plasma bicarbonate remained within normal limits, and the amount of bicarbonate in the urine became less. Throughout that time weight gain was unsatisfactory and the skin elasticity had not become quite normal.

PRESENT CONDITION

All therapy was stopped on Aug. 7, at the age of $15^1/_2$ months. On Aug. 13 the plasma bicarbonate was 51·6 volumes %. The child was discharged home on Aug. 18 aged 16 months and weighing 16 lb. $3^1/_2$ oz.

When seen in the outpatient department on Sept. 22 at the age of 17 months she weighed 18 lb. 13 oz. She had seven teeth, could walk holding on to things, and had been taking her food well. The skin elasticity was normal. Her plasma-bicarbonate level was 45·5 volumes % and her urinary bicarbonate 19·8 volumes %.

On Oct. 4, at the age of $17^1/_2$ months, the child weighed 19 lb. Her plasma bicarbonate was 52·5 volumes % and urinary bicarbonate 4 volumes %.

On Jan. 11, 1949, at the age of $20^1/_2$ months, she weighed 21 lb. 9 oz., and clinical examination showed no abnormality.

OTHER OBSERVATIONS

Renal Function

1. The *urine* did not contain albumin or sugar.

2. The *blood-urea* remained within normal limits throughout the period of observation, values of 33, 30, 16, 27, 27, 46, 30, and 36 mg. per 100 ml. being found.

3. The *urea clearance* on May 21, at the age of 13 months, gave an absolute value of 14·4 and 12·4 ml. per min. On June 4, at the age of $13^1/_2$ months, the urea clearance was 10, 12, and 14 ml. per min., giving an average clearance of 12 ml. per min. When this is corrected for a surface area of 1·73 sq. m., as suggested by Schoenthal et al. (1933), it gives a clearance of 79 and 68 ml. per min.

4. The *specific gravity of the urine* varied from 1·005 to 1·014. Most of the readings were 1·008. An attempt to perform a urine concentration test by withholding fluid was unsuccessful for technical reasons.

5. The urinary *chlorides* varied from 130 to 440 mg. per 100 ml. in random samples. In view of the observation that Albright's patient (Albright et al. 1940) was made more acidotic by the administration of sodium chloride, the effect of physiological saline solution 105 ml. three times a day for three days was observed. There was no significant alteration in plasma or urinary bicarbonate or in the specific gravity of the urine.

Chlorides of Cerebrospinal Fluid

Before the condition was recognised, the C.S.F. was examined on March 17 and April 7. The chloride levels were 860 and 840 mg. per 100 ml. respectively, which probably were due to a high plasma-chloride level at that time. In fact on the latter occasion the plasma chloride the same day was 780 mg. per 100 ml.

DR. SOMMERVILLE AND OTHERS: REFERENCES—*continued*

Sommerville, I. F., Gough, N., Marrian, G. F. (1948) *J. Endocrinol.* **5**, 247.
Stevenson, M. F., Marrian, G. F. (1947) *Biochem. J.* **41**, 507.
Strickler, H. S., Shaffer, C. B., Wilson, D. A., Strickler, E. W. (1943) *J. biol. Chem.* **148**, 251.
Venning, E. H. (1937) *Ibid*, **119**, 473.
— (1938) *Ibid*, **126**, 595.

Digitized by Google

TABLE I—BLOOD CHEMISTRY DURING AND AFTER ALKALI THERAPY

Constituent	April 7, after 2 weeks on M/6 lactate 180 ml. daily by mouth	April 14, after 3 weeks on M/6 lactate 180 ml.	April 15, 44 hours after lactate had been stopped	April 26, after 1 week on M/6 lactate 380 ml.	May 3, after 2 weeks on M/6 lactate 380 ml.	Oct. 4, 8 weeks after cessation of alkali therapy
Sodium						
(mg. per 100 ml.)	..	370	350	..	335	315
(m. eq. per litre)	..	161	152	..	145	137
Bicarbonate						
(CO_2 combining power vols. %)	37	38·1	..	35·2	30·9	52·5
(m. eq. per litre)	17	16·6	..	15·8	14	24
Chloride						
(mg. per 100 ml. as NaCl)	780	700	740	666	690	660
(m. eq. per litre)	133	120	129	115	120	114
Protein						
(g. per 100 ml.)	7·3	8·4	9·0	7·0	7·3	6·1
(Base eq. as m. eq.—i.e., × 2·43)	17·7	20·4	21·9	17·0	17·7	14·8

Methods: serum-chloride (Harrison 1947, p. 346); serum-sodium (Harrison 1947, p. 389); serum proteins by micro-Kjeldahl.

Calcium and Phosphorus

The serum-calcium was 12·7 mg. per 100 ml. on April 19, and 11·1 mg. on May 3, and 12·2 mg. on Oct. 4. The serum-inorganic phosphorus was 5·3 mg. per 100 ml. on May 3.

Blood-counts

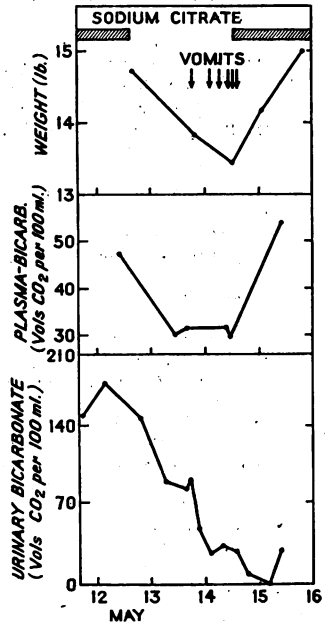
The red-cell count varied between 3,900,000 and 4,900,000 per c.mm., and the hæmoglobin from 7·9 to 11·3 g. per 100 ml. There was no abnormal leucocyte-count at any time.

Carbohydrate Metabolism

On May 12, at the age of $12^1/_2$ months, blood-sugar values were 79 and 101 mg. per 100 ml. At no time was there any glycosuria, and no ketonuria was observed.

Radiography

Radiography of wrists and abdomen on March 26, April 2, and Nov. 2 showed no evidence of rickets or of renal calcification.



Changes after cessation of alkali medication during active stage of illness.

DIET

The child was throughout offered a normal diet for her age; she was given 'Adexolin' minims 10 daily and ascorbic acid 50 mg. twice a day during her stay in hospital. While at home she had $1^1/_2$ teaspoonfuls of cod-liver oil and two teaspoonfuls of concentrated orange juice daily.

PREVIOUS RECORDS

Lightwood (1935) found at necropsy insoluble calcium salts in the renal tubules in 6 infants, aged from five to eleven months, who had all presented certain common clinical features.

Payne (1948) observed 7 further cases during life. All the children were under one year of age and had an illness of over four weeks' duration, with anorexia, constipation, loss of weight, vomiting, hypotonia, and alteration in skin elasticity. The urine contained leucocytes, epithelial cells, and often a trace of albumin, and it was often alkaline. They all showed a persistently low plasma-carbon-dioxide combining power, and the serum-chloride levels were raised higher than would be caused by the degree of acidosis. Payne regarded the presence of an alkaline urine with persistent acidosis as of diagnostic value. The infants were treated with the sodium citrate-citric acid mixture of Albright et al. (1940), which caused clinical improvement and corrected the acidosis.

Butler et al. (1936) reported a group of 4 infants who showed persistent dehydration and low plasma-bicarbonate and high plasma-chloride levels. They associated the condition with the necropsy finding of calcification in and around the renal tubules.

MacGregor (1948) analysed the case-histories of 25 children, all under the age of two years, who showed calcification in the medulla of the kidneys at necropsy, and he found that 18 of them could be classified as belonging to the group described by Lightwood (1935). He also examined 230 kidneys of children, under two years of age, dying from other causes and found similar calcification in 11%. He concluded that precisely similar calcification was to be found in many different and apparently unrelated conditions in this age-group.

Hartmann (1939) reported the case of a male infant who, at the age of two months, began to have bouts of vomiting, sometimes accompanied by dyspnœa. When seen after such a bout, at the age of four months, the infant had severe acidosis, which was effectually treated with parenteral sodium-r-lactate. The acidosis recurred when the lactate was stopped, and then the urine was studied. The urine had a hydrogen-ion concentration approximately that of blood, though at the same time the plasma-carbon-dioxide combining power was low. Occasionally a trace of albumin was found in the urine, but there was a normal ability of the kidney to clear the blood of urea and to excrete phenolsulphonephthalein. In fact, the only clear evidence of renal disorder was the persistent excretion of bicarbonate in the urine even in the presence of a low plasma-carbon-dioxide combining power. The acidosis was corrected by the administration of sodium-r-lactate by mouth. At the age of eleven months the lactate was stopped without ill effect. The infant was seen again at the age of sixteen months, when he seemed normal in all respects.

Albright et al. (1940) reported the case of a girl, aged thirteen years, with persistent rickets and dwarfism. They compared the case with a boy, aged ten years, observed by Butler et al. (1936) and considered the cases to be similar. There was a low alkali reserve in the plasma, a high plasma-chloride level, and an inability to secrete an acid urine. The condition was associated with severe and probably secondary disturbances of calcium metabolism. The case observed by Albright et al. (1940) showed a rise in the serum-carbon-dioxide combining power and a lowering of the serum-chloride level following the administration of a sodium citrate-citric acid mixture. They concluded that there was a decreased ability of the renal tubules to excrete an acid urine or to make ammonia.

Baines et al. (1945) reported the case of a woman, aged twenty-nine, with polyuria, bilateral renal stones, a raised serum-chloride level, a low plasma-bicarbonate level, and urine of relatively fixed specific gravity and hydrogen-ion concentration, the pH varying between 6·7 and 8·1. She was improved by the administration of a sodium-citrate-citric acid mixture by mouth. They concluded that there was an inability of the tubules to form sufficient ammonia to allow the excretion of acid radicals without the loss of vital basic elements.

DISCUSSION

The present case seems to be of the same type as those of Lightwood (1935), Butler et al. (1936), Hartmann (1939), and Payne (1948).

An alkaline urine in the presence of a low plasma-carbon-dioxide combining power might be due either to

Digitized by Google

an inability to conserve bicarbonate by the renal tubules or to an inability to form ammonia. In view of the quantitative aspects of the mechanisms for conserving alkali (Pitts 1945), a failure of bicarbonate reabsorption seems much more likely than merely an inability to form ammonia. Though no observations were made on the excretion of ammonia in the urine, the striking feature has been the continued excretion of bicarbonate in the presence of a low plasma-carbon-dioxide combining power.

TABLE II—RELATIONSHIP BETWEEN DAILY DOSE OF SODIUM CITRATE AND BICARBONATE IN PLASMA AND URINE

Date	Time	Daily dose of alkali	Plasma bicarbonate (vols. %)	Urinary bicarbonate (vols. %)
May 9	—	Sodium citrate 6 g.		135
May 11	4·50 P.M.			148
May 12	3.00 A.M.			178
	7.50 A.M.			166
	10.00 A.M.		47	
	2.30 P.M.			
	6.15 P.M.			148
	10.00 P.M.			128
May 13	7.15 A.M.			95
	9.30 A.M.			106
	10.10 A.M.		29·4	
	2.00 P.M.			87
	3.00 P.M.			86
	3.50 P.M.		30·8	
	6.30 P.M.			94
	9.30 P.M.			51·1
May 14	3.00 A.M.			31
	6.00 A.M.			35·5
	9.00 A.M.		30·9	
	12.30 P.M.		29·4	
	1.00 P.M.	Sodium citrate 6 g.		29·2
	7.10 P.M.			11·3
May 15	5.30 A.M.			0
	9.00 A.M.		54·5	
	9.30 A.M.			27·5
May 18	7.00 A.M.			55·5
May 19	9.30 A.M.		46·8	
	1.00 P.M.			56
May 22	6.15 A.M.	Sodium citrate 4 g.		23·2
	7.30 A.M.			28·0
	9.05 A.M.		41·7	
May 24	2.50 P.M.	Sodium citrate 8 g.		58
	5.50 P.M.			116·4
	7.05 P.M.			135·4
May 25	4.10 A.M.			102·0
	7.35 A.M.			36·5
May 27	8.30 A.M.			66·0
	—		53·9	
	9.40 A.M.			75·1
May 31	8.15 A.M.			166·5
	9.25 A.M.		52·8	
June 7	1.50 P.M.			72
	3.50 P.M.			93
	4.05 P.M.		38·0	
June 9	3.00 P.M.			56
	3.45 P.M.		46·9	
June 17	—		37·0	37·5
June 28	7.30 A.M.			7·5
	8.20 A.M.		42·5	17·8
July 2				
July 6	—	Sodium citrate 16 g.	54	68
July 12			47·5	137
July 19				
July 21	—		46·2	4
July 30		Sodium citrate 8 g.		
Aug. 4	9.00 A.M.		49·1	72·7
Aug. 7	9.00 A.M.			54
Aug. 13	2.00 P.M.		51·6	5·4
Sept. 21	11.15 A.M.		43·5	19·8
Oct. 4			52·5	4·0

Determination of plasma bicarbonate and urinary bicarbonate.—Venous blood was collected in a small tube containing oxalate with fluoride and centrifuged under liquid paraffin after saturation with a gas mixture containing 5% carbon dioxide and 95% oxygen. Bicarbonate was determined manometrically in 0·1 or 0·2 ml. of plasma (Warburg 1930). Urinary bicarbonate was determined by the same method. The gas space of the manometer vessels contained 5% carbon dioxide and 95% oxygen in both the blood and urine analyses.

Normally, on an acid-ash diet the bicarbonate which is present in the glomerular filtrate is conserved and only very small amounts are lost in the urine if the plasma-bicarbonate level is low. If, however, alkali is administered so that supplies of available base exceed the needs of the body, the excess of base is excreted in the urine as bicarbonate. The conservation of bicarbonate by the tubules constitutes the main means of preventing depletion of the alkali reserve of the body (Pitts and Lotspeich 1946). The administration of sulphanilamide reduces the capacity of the kidney to conserve bicarbonate. Pitts inferred that the additional excretion of bicarbonate after administration of sulphanilamide was due to a disturbance in the distal tubular exchange of H^+ ions for Na^+ ions, probably because sulphanilamide interferes with the enzyme carbonic anhydrase. Sulphanilamide did not effect the reabsorption or excretion of chloride.

It is possible that the enzyme carbonic anhydrase is inhibited or that there is a failure of the mechanism for secreting hydrogen ions (Davies and Roughton 1948, Davies 1949), but one cannot, on the evidence available, go further than to say that there is a functional disorder involving the mechanism for the conservation of bicarbonate.

The clinical importance of the syndrome described is twofold: (1) its recognition as a cause of chronic failure to thrive in infancy; and (2) the fact that the disturbance appears to be sometimes temporary and that administration of alkali by mouth may compensate for the loss of bicarbonate in the urine until recovery takes place.

SUMMARY

A case is described of an infant with vomiting, constipation, and persistent acidosis.

Investigation showed the excretion of bicarbonate in the urine in the presence of a low plasma-bicarbonate level.

The condition responded to administration of alkali by mouth.

It is suggested that the underlying disorder is a temporary failure of bicarbonate reabsorption by the renal tubules.

The early recognition of the condition depends on estimations of both plasma bicarbonate and urinary bicarbonate.

I would like to express my indebtedness to Prof. H. A. Krebs, in whose laboratory the bicarbonate estimations in blood and urine were made, for advice; to Dr. A. Jordan, in whose laboratory the other biochemical estimations were made for his criticism and encouragement; to Dr. D. R. Wood, Dr. S. Doxiadis, and Dr. J. Burke for assistance; and to Prof R. S. Illingworth, who was in charge of the case.

REFERENCES

Albright, F., Consolazio, W. V., Coombs, F. S., Sulkowitch, H. W., Talbott, J. H. (1940) *Bull. Johns Hopk. Hosp.* **66**, 7.
Baines, G. H., Barclay, J. A., Cooke, W. T. (1945) *Quart. J. Med.* **14**, 113.
Butler, A. M., Wilson, J. L., Farber, S. (1936) *J. Pediat.* **8**, 489.
Davies, R. E. (1949) *J. Physiol.* **108**, 25P.
— Roughton, F. J. W. (1948) *Biochem. J.* **42**, 609.
Harrison, G. A. (1947) Chemical Methods in Clinical Medicine. 3rd ed., London.
Hartmann, A. F. (1939) *Ann. intern. Med.* **13**, 940.
— Perley, A. M., Basman, J., Nelson, M. V., Asher, C. (1938) *J. Pediat.* **13**, 692.
Lightwood, R. (1935) *Arch. Dis. Childh.* **10**, 205.
MacGregor, M. E. (1948) *Ibid*, **23**, 145.
Payne, W. W. (1948) *Ibid*, p. 145.
Peterman, M. G. (1945) *Amer. J. Dis. Child.* **69**, 291.
Pitts, R. F. (1945) *Science*, **102**, 49, 81.
— Lotspeich, W. D. (1946) *Amer. J. Phys.* **147**, 138, 481.
Schoenthal, L., Lurie, D., Kelly, M. (1933) *Amer. J. Dis. Child.* **45**, 41.
Warburg, O. (1930) The Metabolism of Tumours. London.

Digitized by Google

PREPARATION AND STANDARDISATION OF SACCHARATED IRON OXIDE FOR INTRAVENOUS ADMINISTRATION

JOSEPH A. NISSIM
M.B. Lond.
DEMONSTRATOR IN PHARMACOLOGY

J. M. ROBSON
M.D., D.Sc. Leeds, F.R.S.E.
READER IN PHARMACOLOGY

IN THE UNIVERSITY OF LONDON, AT GUY'S HOSPITAL MEDICAL SCHOOL

IT has been shown (Nissim 1947) that saccharated iron oxide can be given intravenously in man. It was observed, however, that different samples had widely different toxicities, and this was soon confirmed by Asher (1947), who noted severe toxic reactions in two patients. Asher's sample proved on inspection to be only partially in solution, whereas the original sample was perfectly clear. Obviously the method of preparation of saccharated iron oxide needed standardisation, and a biological assay of toxicity was necessary.

This object has been achieved, and a method has been found which enables the preparation of saccharated iron oxide to be controlled to a nicety. This same method also led to the preparation of better samples.

Mackenzie (1913) states that sucrose or saccharose forms a compound with ferric hydroxide known as iron sucrate or saccharate. It can be prepared in various ways. Ferric hydroxide is mixed with sugar and water, and this gives a solution of iron sucrate on addition of sodium hydroxide. In some cases the product is entirely soluble in water, in others only partially.

Preliminary experiments showed that the properties of ferric hydroxides prepared by different methods varied, and that the sucrates formed from them differed widely in the amount of alkali needed to dissolve them. The ferric hydroxide obtained by adding sodium hydroxide to ferric chloride yielded a sparingly soluble sucrate. That obtained by adding ferric chloride to sodium carbonate gave far better results, which, however, depended essentially on the relative amounts of the two reacting substances. In this reaction, represented by the following equation, it appears that ferric carbonate is produced first, but this soon hydrolyses in water giving ferric hydroxide:

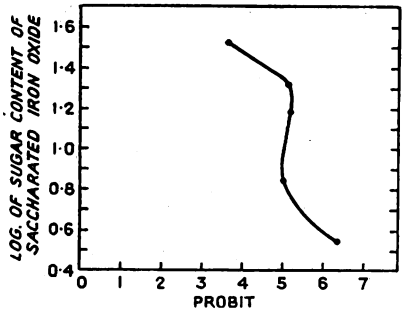


Fig. 1—Relation between logarithm of sugar content of samples of saccharated iron oxide and their toxicity (expressed as probits of percentage survivals).

$$2FeCl_3 + 3Na_2CO_3 \longrightarrow 6NaCl + Fe_2(CO_3)_3$$
$$Fe_2(CO_3)_3 + 6H_2O \longrightarrow 2Fe(OH)_3 + 3H_2CO_3$$

The carbonate may be got rid of either by repeated washing with water or by driving it off as carbon dioxide by bringing the pH to the acid side. Both these procedures increase the solubility of the sucrate, but the best ferric hydroxide—i.e., the one giving the most soluble sucrate—was produced by dissolving the ferric hydroxide in excess of ferric chloride and reprecipitating it with sodium carbonate.

METHOD OF PREPARATION

Figures are given for a quantity of saccharated iron oxide containing 10 g. of elemental iron, after allowing for a loss in the process of about 0·25 g. of iron (2·5%). All substances used were of Analar standard.

Anhydrous sodium carbonate 25 g. is dissolved in a litre of distilled water and 50 g. of $FeCl_3.6H_2O$ is added. Carbon dioxide is evolved, and the ferric hydroxide thus formed dissolves in the excess of ferric chloride to give a dark purple solution. This can be aided by occasional shaking. Saturated sodium carbonate solution is then added gradually to reprecipitate all the iron as ferric hydroxide, and this is ensured by bringing the pH up to 7.

The sodium chloride formed as a by-product of the reaction is washed away by repeatedly adding distilled water in quantities of 1000–2000 ml. at a time, allowing the ferric hydroxide to settle, and decanting. This is continued until the supernatant fluid first begins to acquire a brownish tinge. The colour is due to the failure of the ferric hydroxide to settle down completely from the supernatant fluid which now contains little electrolyte.

After decanting or siphoning off for the last time, 166 g. of sucrose is added, followed by 30 ml. of 15% NaOH (0·45 g. of NaOH per g. of iron). This brings the pH to about 11·7. The mixture is next poured into a flat enamel or porcelain dish and placed in the oven at a temperature of 130°C. The saccharated hydroxide gradually dissolves to an almost black solution.

If a sample of this alkaline solution is now taken—just enough to colour 10 ml. of distilled water red brown—and

TABLE I—RESULTS OF TOXICITY TESTS IN MICE WITH VARIOUS PREPARATIONS OF SACCHARATED IRON OXIDE AND WITH IRON AND AMMONIUM CITRATE

Preparation	No. of mice	Dose (mg. of iron per kg. of body-weight)	No. of mice surviving after 10 days	Equivalent dose for a man weighing 70 kg. (g.)
Sample A (standard) ..	22	180	11 (*50%*)	12·6
,, ..	17	270	6 (*35%*)	18·9
,, ..	1	315	1	22·0
,, ..	2	360	0	25·2
,, ..	3	450	0	31·5
Sample B (replica of standard)	20	180	12 (*60%*)	12·6
Sample B (neutralised) ..	10	180	6 (*60%*)	12·6
Sample C (same as sample B but without carbonate) ..	10	180	6 (*60%*)	12·6
Sample D (same as sample C but sugar only 16·6 g. per g. of iron, none added after evaporation) ..	20	180	11 (*55%*)	12·6
Sample E (same as D but non-reprecipitated hydroxide used) ..	10	180	1 (*10%*)	12·6
Samples F1–F4 (same as sample D except for sugar content):				
Sample F1 (33·3 g. of sucrose per g. of iron)	10	180	0	12·6
Sample F2 (21·6 g. of sucrose per g. of iron)	10	180	1 (*10%*)	12·6
Sample F3 (6·6 g. of sucrose per g. of iron)	10	180	5 (*50%*)	12·6
Sample F4 (3·3 g. of sucrose per g. of iron)	20	180	18 (*90%*)	12·6
Samples G1–G4 (same as sample D but for precipitation point):				
Sample G1 (p.p. = 6·5) ..	10	180	0	12·6
Sample G2 (p.p. = 6·0) ..	10	180	1 (*10%*)	12·6
Sample G3 (p.p. = 4·7) ..	10	180	10 (*100%*)	12·6
Sample G4 (p.p. = 3·7) ..	20	180	20 (*100%*)	12·6
	30	270	22 (*73%*)	18·9
	10	360	1 (*10%*)	25·2
Samples H1 and H2 (same as F3 except for precipitation point):				
Sample H1 (p.p. = 4·7) ..	10	180	9 (*90%*)	12·6
Sample H2 (p.p. = 3·7) ..	10	270	6 (*60%*)	18·9
	10	360	1 (*10%*)	25·2
Sample I (3·3% sugar, p.p. 4·7)	5	180	0	12·6
Iron and ammonium citrate	1	180	0	12·6
	1	135	0	9·45
	2	90	0	6·3
	2	45	0	3·15
	7	22·5	0	1·58
	4	11·25	4 (*100%*)	0·8

Digitized by Google

TABLE II—DETAILS OF SAMPLES OF SACCHARATED IRON OXIDE USED IN TOXICITY TESTS OF TABLE I

Sample	pH	Carbonate content (g. of Na_2CO_3 per g. of iron)	Sucrose added after evaporation to dryness (g. per g. of iron)	Sucrose added before evaporation to dryness (g. per g. of iron)	Type of hydroxide	pH of precipitation point
A	10·8	1·0	About 15	16·6	Not known	5·7
B	10·8	1·0	15	16·6	Reprecipitated	5·7
B neutralised	7·3	1·0	15	16·6	,,	5·7
C	11·0	0	15	16·6	,,	5·7
D	11·0	0	0	16·6	,,	5·7
E	11·0	0	0	16·6	Non-reprecipitated	5·7
F1	11·0	0	0	33·3	Reprecipitated	5·7
F2	11·0	0	0	21·6	,,	5·7
F3	11·0	0	0	6·6	,,	5·7
F4	11·0	0	0	3·3	,,	5·7
G1	11·0	0	0	16·6	,,	6·5
G2	11·0	0	0	16·6	,,	6·0
G3	11·0	0	0	16·6	,,	4·7
G4	11·0	0	0	16·6	,,	3·7
H1	11·0	0	0	6·6	,,	4·7
H2	11·0	0	0	6·6	,,	3·7
I	11·0	0	0	3·3	,,	4·7

dilute hydrochloric acid is added to it drop by drop, it precipitates when a pH of 8 is reached. It was found that the pH at which this precipitation takes place falls gradually under the continued action of heat, and samples with precipitation points between pH 8 and pH 3 may be obtained. The original specimen used clinically with success had a precipitation point of pH 5·7, and consequently the first samples prepared during this investigation were made to correspond to this. Samples precipitating at other pH were also prepared and studied.

When the required precipitation point is reached, the temperature of the oven is brought down to 90°C, and, if not already dry, the final product is evaporated to dryness.

The saccharated iron oxide thus formed is dissolved in 500 ml. of distilled water to give a solution containing 2% elemental iron. It is filtered through a Whatman no. 50 filter paper and autoclaved at a pressure of 10 lb. per square inch, or a temperature of 115–116°C, for half an hour. It is now ready for use.

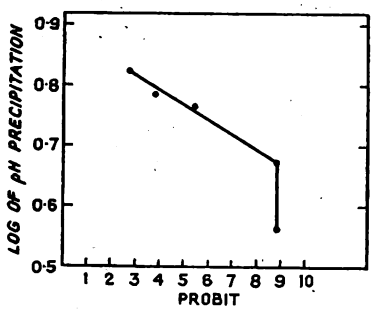


Fig. 2—Relation between pH of precipitation (log. scale) of samples of saccharated iron oxide and their toxicity (expressed as probits of percentage survivals).

DIFFERENT TYPES OF SACCHARATED IRON OXIDE

It was found that the amount of alkali, sucrose, and carbonate could be varied as well as the pH of the precipitation point. Each of these factors was studied independently.

Alkali Content.—Though saccharated iron oxide can be prepared with smaller quantities of sodium hydroxide, precipitation takes place during autoclaving if the pH of the solution is below 10·5. So far clinical experience has been limited to alkaline solutions of saccharated iron oxide, but neutral solutions used in experiments on animals have been obtained by autoclaving the requisite amounts of hydrochloric acid and saccharated iron oxide in separate bottles and mixing before injection.

Sucrose Content.—Saccharated iron oxide may be formed with proportions of sugar ranging from as little as 3·3 to over 33·3 g. per g. of iron. The samples with the lower sugar content have the advantage of being less viscid. Those containing less sucrose than 6·6 g. per g. of iron precipitate when autoclaved in solution, whatever their pH.

Carbonate Content.—The carbonate content of the saccharated iron-oxide samples prepared as described above is negligible, since what is not driven off as carbon dioxide is washed away with the sodium chloride. However, commercial samples were found to vary in their carbonate content (see below), and the effect of the carbonate content on the toxicity was therefore studied, and the results are included in the toxicity tests described below.

A specimen of saccharated iron oxide (B.D.H.) used in the original experiments (Nissim 1947) had a pH of 10·75 as a solution containing 1% of Fe, and 11 as a 0·1% solution. The powder had a carbonate content of 3% as Na_2CO_3 (Van Slyke method)—i.e., about 1 g. of Na_2CO_3 per g. of iron. This would correspond to 2·22 g. of NaOH per 100 g. of the powder, which presumably was originally added as sodium hydroxide and later became converted to Na_2CO_3 by absorption of CO_2 from the air. The total alkali content was estimated as 2·7 g. of NaOH per 100 g. of the powder, methyl orange being the indicator. The iron content was 2·9%, and the pH of precipitation on addition of hydrochloric acid was 5·7. As regards sugar content, British Drug Houses inform us that their method of preparation involves the addition of 50% sucrose before evaporation to dryness. It is made up to 100% by the further addition of sucrose after evaporation.

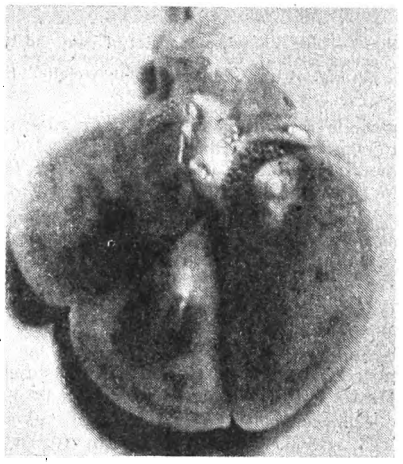


Fig. 3—Hæmorrhages in lungs of mouse injected intravenously with saccharated iron oxide 270 mg. of iron per kg. of body-weight. (× 3.)

TOXICITY TESTS

It is obvious from the summary given here of the methods of preparation of saccharated iron oxide that samples of it may vary in alkalinity, carbonate content, amount of sucrose added before and after evaporating to dryness, type of ferric hydroxide used in the preparation, and pH at which precipitation takes place on addition of hydrochloric acid. Toxicity tests would therefore have to deal with each of those variables independently. In what follows a brief account is given of toxicity tests carried out on the original sample from British Drug Houses (sample A), as well as samples prepared here to investigate the effect of these variables. In addition, iron and ammonium citrate was also tested for comparison. Female white mice all obtained from the same dealer were used. Most of them weighed 25–35 g., but occasionally heavier or lighter ones were used.

Standard (sample A).—Since this preparation was successfully used in clinical work, it seemed desirable to use it as a standard with which other preparations could be compared. Its L.D.50 when given intravenously to mice was about 180 mg. of iron per kg. of body-weight, which is equivalent to 12·6 g. of iron for a man weighing 70 kg. With this dose the mice did not die immediately after injection, but after

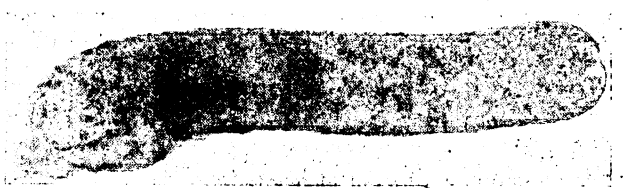


Fig. 4—Hæmorrhages in appendix of rabbit injected intravenously with saccharated iron oxide 360 mg. of iron per kg. of body-weight. (About half size.)

Digitized by Google

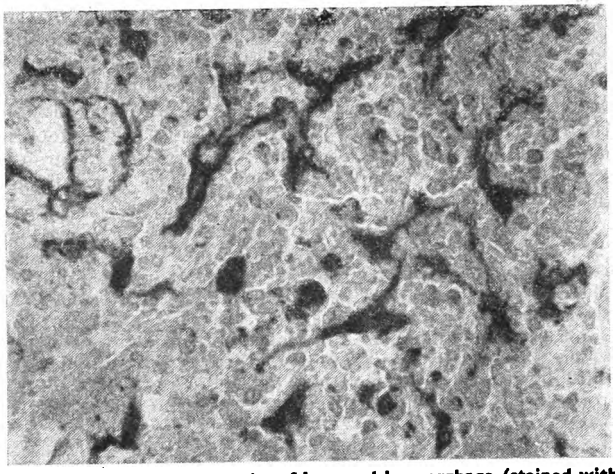


Fig. 5—Lung, showing deposits of iron and hæmorrhage (stained with prussian-blue) in mouse injected with saccharated iron oxide 180 mg. of iron per kg. of body-weight. (× 410.)

periods ranging from one hour to several days. Two mice injected with 450 mg. of iron per kg. of body-weight, however, died immediately after the injection. Table I gives a summary of the toxicity tests for the various samples.

Replica of standard (sample B).—An exact replica of sample A was prepared even as regards carbonate content (actually added as Na_2CO_3 after washing the ferric hydroxide). Its L.D.50 was practically the same as that of the standard.

Neutralised sample B (pH 7·3).—This had the same toxicity as sample B.

Sample C.—This was the same as sample B except that no carbonate was added after washing the ferric hydroxide. Its toxicity was the same as the previous three samples.

Sample D.—This was the same as sample C, but no sugar was added after evaporating to dryness. There was no alteration in toxicity as a result of this omission. Moreover the viscosity of the resultant solution was reduced, which made it possible to use 2% iron solutions for injection instead of the original 1%.

Sample E.—The only difference from sample D was that the ferric hydroxide was not reprecipitated from excess ferric chloride as described above. The result suggests an increase in toxicity.

Samples F1–F4.—These were the same as sample D, but their sucrose content varied from 3·3 to 33·3 g. per g. of iron (table I). All these samples had a precipitation point of 5·7. It is seen that the toxicity dropped with the sugar content, but the relationship is not linear, even when the logarithm of sugar content is plotted against the probit of survival (fig. 1).

Samples G1–G4.—The toxicity of samples with precipitation point between 6·5 and 3·7 was also tested (table I and fig. 2). All these samples had a sucrose content of 16·6 g. per g. of iron. The logarithm of the precipitation point plotted against the probit of survival of the mice gives a linear relationship. The sudden bend in the graph at pH 4·7 is merely due to the maximal survival being reached with that dose. The best sample had a precipitation point of 3·7 and an L.D.50 of about 300 mg. of iron per kg. of body-weight. Below 3·7, samples were partially charred, gave a precipitate on standing, and proved more toxic. Sample H2 with a sucrose content of 6·6 g. per g. of iron and a precipitation point of 3·7 had about the same L.D.50 of 300 mg. of iron per kg. of body-weight, but have not yet been tried clinically. Samples with low pH of precipitation—e.g., 3·7—also showed a fall in the pH of the solution, from 11·7 to about 10·0 or slightly lower. This should be restored to 11·0 or 11·2 by addition of sodium hydroxide before autoclaving.

Iron and ammonium citrate.—This compound is about fifteen times as toxic as saccharated iron oxide (table I).

CLINICAL TRIALS

The sample of saccharated iron oxide with 16·6 g. of sucrose per g. of iron and a precipitation point of 3·7 was tried clinically. Several patients received repeated doses of as much as 300 mg. of iron by intravenous injection without the slightest toxic reaction. Each of these injections is equivalent in iron content to $1^1/_2$ pints of blood. Even larger doses may possibly be tolerated.

NECROPSY FINDINGS IN MICE

Mice given lethal doses of saccharated oxide of iron almost invariably showed macroscopic hæmorrhagic lesions. These were most notable in the lungs (fig. 3), often giving the gross appearance of infarcts, and sometimes involving a whole lobe. Hæmoptysis was occasionally observed, and was sometimes the immediate cause of death. Intestinal hæmorrhages were relatively frequent (fig. 4), and petechial spots were especially marked in the cæcal area. Lesions were also seen in the liver, kidneys, and heart—in that order of frequency. The few mice in which no macroscopic lesions were observed showed, as did all the other mice, histological evidence of hæmorrhages, mainly in the lungs and liver. Heavy deposits of iron were also present in both of these organs, but notably in the lungs (figs. 5 and 6).

Though, as noted by Cappell (1930), saccharated iron oxide is stable in contact with blood-plasma in doses of 45 mg. of iron per kg. of body-weight, the hæmoptyses, as well as the necropsy findings, suggest that, with the lethal doses used here (4–8 times those given by Cappell), the iron precipitates slowly, and death is presumably due to multiple capillary embolism in internal organs.

Saccharated iron oxide is stable in contact with plasma in vitro. It appears to undergo gradual precipitation

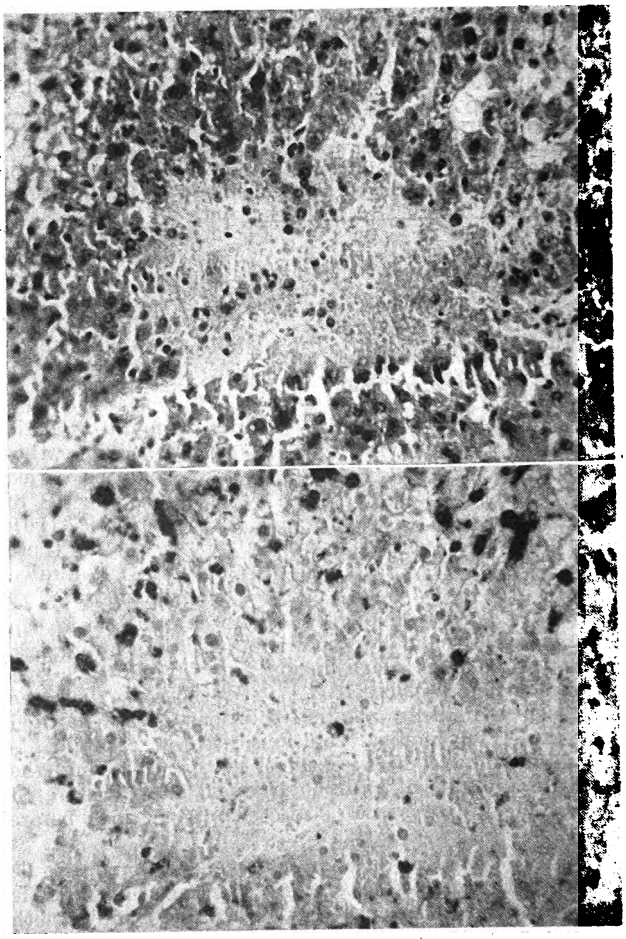


Fig. 6—Liver, showing area of degeneration presumably due to embolism in mouse injected with saccharated iron oxide 180 mg. of iron per kg. of body-weight: above, stained with hæmatoxylin and eosin; below, stained with prussian-blue (note degenerated area is relatively free from iron deposits). (× 230.)

Digitized by Google

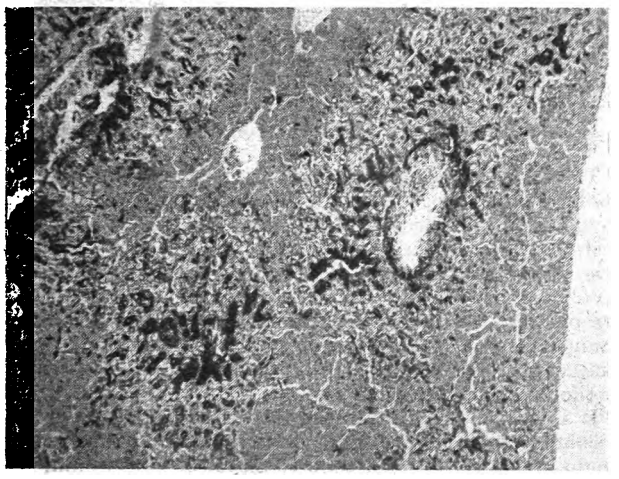


Fig. 7—Liver of mouse which died ½ hour after intravenous injection of saccharated iron oxide 450 mg. of iron per kg. of body-weight. Note iron precipitated in large vessel. (× 80.)

in vivo, however, with the result that animals killed as long as ½–1 hour after a large injection may still show free iron precipitates in large vessels (fig. 7). These must have precipitated at about the time of death, otherwise they would have been caught up in the capillary bed. A possible explanation for this gradual precipitation is the breakdown of the compound as the sugar part of the molecule is metabolised. The toxicity of saccharated iron oxide would thus be directly proportional to its rate of metabolism and inversely proportional to the rate at which it can be removed from the blood by the reticulo-endothelial system.

It may be recalled here that mice injected with 450 mg. of iron in sample A per kg. of body-weight died immediately after the injection. If precipitation after metabolism were the only cause of the toxic effects of iron saccharate, some period ought to have elapsed before death was produced in spite of the size of the dose. Before attributing some other specific toxic action to this compound it was felt that other possible factors should be taken into account. A control group of three mice injected with the alkali and sucrose equivalent of this dose died immediately as well. When, at a later date, a sample of saccharated iron oxide was prepared containing only 6·66 g. of sucrose per g. of iron, and of neutral reaction, doses as high as 540, 630, and even 900 mg. of iron per kg. of body-weight did not kill in less than ½–2 hours. It is to be noted that the dose of 900 mg. of iron per kg. of body-weight is equivalent to 63 g. per man weighing 70 kg., a dose that would exert a dangerous osmotic effect even if it were ordinary salt. There is thus as yet no evidence that the toxic effects produced by the intravenous administration of saccharated iron oxide are due to any other mechanism besides that of precipitation.

The toxic effects of iron and ammonium citrate and other iron compounds are more complex.

CONCLUSION

It is obvious that, for the time being, preparations of saccharated iron oxide used clinically will have to be standardised biologically to ensure that their toxicity is not too high. In the present work the original sample A was throughout used as standard with which new preparations were compared. It may well be that such a standard will have to be established in the future for testing preparations intended for clinical use. Eventually it may be found that the method of preparation is sufficiently reliable to ensure the constant production of satisfactory samples which will not need biological standardisation.

SUMMARY

A method for the preparation and biological standardisation of saccharated iron oxide in a form suitable for intravenous administration is described.

Variations in the method of preparation are discussed, and an account is given of toxicity tests with these preparations leading to the selection of the best samples for intravenous administration.

The macroscopical and microscopical findings in mice receiving lethal doses are described, and the manner in which saccharated iron oxide produces its toxic effects is discussed.

We thank Prof. Payling Wright and Dr. F. H. Brain for their valuable advice; Mr. J. Moore and Mr. S. F. Izard, who have constantly been helpful in the supply of materials; and Mr. L. A. Westwood, the senior technician in the department, for his coöperation.

REFERENCES

Asher, R. A. J. (1947) personal communication.
Cappell, D. F. (1930) *J. Path. Bact.* 33, 175.
Mackenzie, J. E. (1913) The Sugars and their Simple Derivatives. London.
Nissim, J. A. (1947) *Lancet*, ii, 49.

ANOTHER CASE OF LOUPING-ILL IN MAN

ISOLATION OF THE VIRUS

E. G. BREWIS, M.D. Durh., M.R.C.P. D.P.H.
CHARLES NEUBAUER, M.D. Durh.
OF THE WALKER GATE HOSPITAL, NEWCASTLE-ON-TYNE
E. WESTON HURST, M.D., D.Sc. Birm., F.R.C.P.
HEAD OF SUBDIVISION OF MICRO-ORGANISMAL RESEARCH, IMPERIAL CHEMICAL (PHARMACEUTICALS) LTD.

IN 1930 Pool et al. isolated the virus of louping-ill from sheep, and in 1934 Rivers and Schwentker described cases of laboratory infection in man, but it is only recently that Davison et al. (1948) have drawn attention to the human disease in the field and reported 2 examples of presumably natural infection.

We report here a further case of natural infection, diagnosed clinically, and confirmed by subsequent isolation of the virus. The case occurred in the late spring, when louping-ill was naturally prevalent among sheep, owing to the increased seasonal activity of the sheep tick, *Ixodes ricinus*.

A boy of 17, who worked as a shepherd on the Otterburn Hills when louping-ill was widespread in his flock and many lambs were dying of it, had previously complained that the sheep were full of ticks and that he himself was much troubled by them.

He was admitted to hospital on May 14 with a tentative diagnosis of either meningococcal meningitis or uræmia. The history, ascertained from the parents and the family doctor, was that on May 3 and 4 the boy complained of pain in his neck along the sternomastoid muscles, with some tenderness of the glands on pressure. There was no pyrexia and no sore throat, and he was well again between May 4 and 11. On May 11 he went up to the hills to tend his sheep and should have returned about noon; he did not do so until 5 P.M., when he said he had been sick several times and had fallen asleep. He was put to bed, but nothing definite was found by his doctor. Next day the boy's temperature was 102·4°F and he complained of a sore neck, pain in the back, dizziness, and vomiting, but was still rational. Nothing was prescribed then, but next day his temperature was 103·2°F, he was drowsy, and his condition had deteriorated rapidly; he had passed very little urine since the previous day.

Subsequently the patient related that on May 11 he felt sick when he got to the top of the hill and could not walk

Digitized by Google

TABLE I—FINDINGS IN CEREBROSPINAL FLUID

Date	Colour	Coagulum	Cells per c.mm.	Lymphocytes %	Polymorphs %	Chlorides (mg. per 100 ml.)	Sugar (mg. per 100 ml.)	Protein (mg. per 100 ml.)	Globulin
May 18	clear, slightly yellow	None	177	52	48	650	75	100	++
May 27	clear, colourless	,,	113	57	43	690	75	120	++
June 8	,,	,,	21	54	46	720	65	95	++

straight; he was zigzagging, everything was spinning, and he could not see properly. He then fell asleep, awoke late in the afternoon, and went home, being sick several times on the way and having difficulty in walking. He remembered the doctor coming to see him on two occasions, but he did not remember anything after that until he had been in hospital several days.

On admission he was a well-nourished youth of good physique with flushed cheeks and injected conjunctivæ. The skin was hot and moist; no rash was seen, but the trunk was covered with sheep ticks, particularly the axillæ and round the genitals, where many of the ticks were half-buried in the epidermis and not easily dislodged. He was semicomatose, restless, and wildly resistant when disturbed. Neck stiffness and Kernig's sign were well marked, and there was a general increase in muscle tone. The cranial nerves were normal, and there was no nystagmus. The tendon reflexes were all present, but the abdominal and right cremasteric reflex were absent; the plantar reflexes were normal. The distended bladder was catheterised, the urine being normal except for the presence of acetone.

Lumbar puncture under general anæsthesia produced 15 ml. of clear fluid under a pressure of 150 mm. Unfortunately, a cell count was not done on the specimen which was sent for bacteriological examination. It was sterile, and a stained smear of the deposit showed that the cells were mainly lymphocytes. In the light of our previous experience louping-ill was diagnosed, and this specimen of cerebrospinal fluid, together with a sample of blood, was sent to be examined for the virus.

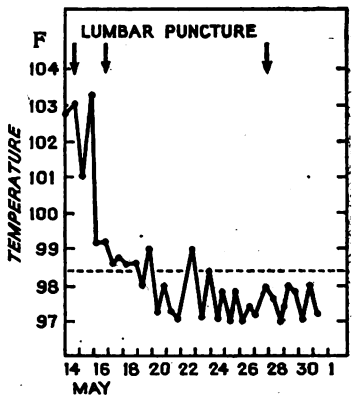
The next day revealed a dramatic change in the patient's condition. From being semicomatose and irrational he was now mentally active and rational, though retarded and without any memory for recent events. Meningeal signs were still present, all tendon reflexes were exaggerated, the abdominal reflexes were now present, and the plantar reflexors still flexor. Speech was so slurred that it was not easy to understand, and there was a fine tremor with ataxia of the upper limbs. There was neither cranial nerve palsy nor papilloedema. Blood-pressure 118/86 mm. Hg. White-cells 9600 per c.mm. (polymorphs 72%, lymphocytes 22%). There was still retention of urine, which persisted until May 19. The temperature subsided by crisis on May 16, and the patient could sit up next day, though neck stiffness still prevented him from putting his chin on his chest, and Kernig's sign remained positive. He felt dizzy, ataxia of the tongue and legs was evident, and there was a definite "clasp-knife" type of spasticity of the limbs.

By May 21 the patient was sitting up, the meningeal signs and spasticity were passing off, the tendon reflexes were less exaggerated, and the ataxia and dysarthria less obvious. White cells 5400 per c.mm. (polymorphs 51%, lymphocytes 45%). Thereafter recovery was rapid, and the patient was discharged from hospital next day, ambulant and well, though there was still tremor of the hands, Rombergism was well-marked, and the tendon reflexes of both upper and lower limbs were very brisk.

The findings in the cerebrospinal fluid (C.S.F.) are shown in table I.

The illness was biphasic, the primary phase occurring about a week before the main illness, showing a similarity to many other virus infections of the central nervous system. The clinical picture was that of acute encephalitis, of short duration and leaving signs of localised involvement of the basal ganglia, mid-brain, and cerebellum, with characteristic cerebellar ataxia. The changes in the C.S.F. were in no way specific and were similar to those found in many cases of virus infection of the nervous system.

It is reasonable to suggest that, had not the patient become semicomatose and delirious for 36 hours, he might never have been sent to hospital and would, no doubt, have been considered an unusual case of influenza or encephalitis lethargica. This is another example of the non-specific character of the clinical illness associated with encephalitis due to other virus infections, and of the inability to differentiate them without adequate laboratory facilities.



Temperature in louping-ill.

Clinical recovery was almost complete, though slight pleocytosis was still present in the C.S.F. and some ataxia was evident. It is of interest in this connexion that our previous patient left hospital also incompletely recovered, and we wondered whether some permanent postencephalitic syndrome might have become established. This man, however, was known to the parents of the present patient, and they informed us that he had recovered so well that he once more was able to follow his occupation as a hill shepherd.

EXPERIMENTAL INVESTIGATION

Table II presents the results of testing the patient's serum for neutralising activity against the virus of louping-ill. The specimen taken shortly after the onset of nervous symptoms already contained antibodies. On intracerebral injection of serum-virus mixtures into mice the titre of the virus was reduced by about two tenfold dilutions. On intramuscular inoculation the mixtures were inactive; all the mice survived and on reinoculation with virus showed no evidence of immunity. The speci-

TABLE II—RESULTS OF TESTING PATIENT'S SERUM FOR NEUTRALISING ACTIVITY AGAINST KNOWN LOUPING-ILL VIRUS

Dilution of virus	Normal horse serum		Patient's sample of May 14		Patient's sample of May 24		Patient's sample of June 29	
	Intracerebral	Intramuscular	Intracerebral	Intramuscular	Intracerebral	Intramuscular	Intracerebral	Intramuscular
10^{-1}	Not tested	8,9,9,9,10,11	Not tested	S,S,S,S,S,S	Not tested	S,S,S,S,S,S	Not tested	S,S,S,S,S,S
10^{-3}	5,5,6,6,6,6	9,10,10,13,S,S	5,6,6,7,7,8	S,S,S,S,S,S	6,6,7,7,7,10	S,S,S,S,S,S	7,7,7,S,S,S	S,S,S,S,S,S
10^{-4}	6,6,6,6,7,7	9,11,12,S,S,S	7,8,9,S,S,S	S,S,S,S,S,S	7,7,S,S,S,S	S,S,S,S,S,S	S,S,S,S,S,S	S,S,S,S,S,S
10^{-6}	8,11,11,15,S,S	Not tested	S,S,S,S,S,S	Not tested	S,S,S,S,S,S	Not tested	S,S,S,S,S,S	Not tested

Equal parts of serum and of the dilutions of virus stated were mixed and allowed to stand 1 hour at room temperature. They were then injected intracerebrally (0·03 ml.) or intramuscularly (0·5 ml.) into mice. The numerals show the days of death of individual mice. S, animal survived.

Digitized by Google

TABLE III—NEUTRALISATION BY VARIOUS SERA OF VIRUS ISOLATED FROM PATIENT

Dilution of virus	Normal horse serum		Patient's serum of June 29		Anti-louping-ill serum	
	Intracerebral	Intramuscular	Intracerebral	Intramuscular	Intracerebral	Intramuscular
10^{-1}	Not tested	7,8,8,9,9,9	Not tested	S,S,S,S,S,S	Not tested	S,S,S,S,S,S
10^{-2}	6,6,6,6,6,6	Not tested	6,6,7,7,7,7	Not tested	5,6,6,6,7,7	Not tested
10^{-3}	Not tested	7,8,8,9,11,12	Not tested	S,S,S,S,S,S	Not tested	S,S,S,S,S,S
10^{-4}	6,6,6,6,6,6	Not tested	7,8,8,9,S,S	Not tested	8,S,S,S,S,S	Not tested

Symbols as in table II.

men of serum taken 10 days later showed about the same degree of activity, but that taken 6 weeks later neutralised roughly a hundred times more virus than did the first. The serum of the patient's father was wholly devoid of neutralising power.

The C.S.F. taken on May 14 was inoculated intracerebrally and intramuscularly into six mice. Five remained well and later showed no immunity to known louping-ill virus. Nine days after inoculation, the sixth mouse was leaping wildly about its cage. It was killed, and the soft and bacteriologically sterile brain was passed to 12 more mice. Two of these developed nervous symptoms on the 13th day; the rest were apparently unaffected, but reinoculated intracerebrally with known louping-ill virus they showed evidence of partial immunity, as indicated by a delayed onset of nervous illness (9–10 days compared with 7 days in controls). In subsequent passages all mice inoculated intracerebrally developed, within 4–9 days, symptoms and lesions indistinguishable from those of louping-ill.

The identity of the pathogenic agent thus isolated was further established by serum-neutralisation and cross-immunity tests. Table III gives the results of serum-neutralisation tests with the patient's serum and the serum of a man who, in 1932, acquired a laboratory infection with louping-ill. Both neutralised the newly isolated virus to about the same extent. In the cross-neutralisation tests groups of 30 mice were inoculated intramuscularly with a 1 : 10,000 dilution of the patient's virus and louping-ill virus. A month later the survivors of each group (6 and 14 mice) were inoculated intramuscularly with a 1 : 10 dilution of the other virus; on this occasion controls of the same weight, age, and batch as the original groups of 30 were similarly inoculated. No nervous disease or mortality occurred among the survivors from the earlier inoculations, whereas 4 of 6 controls given the patient's virus and 6 of 6 given louping-ill virus died.

There is, therefore, every reason to identify the virus isolated from the patient with that of louping-ill. The animals inoculated with the two viruses were housed in separate isolation units between which no possibility of cross-infection existed.

DISCUSSION

The virus of louping-ill is one of a group of pantropic viruses transmitted in nature by blood-sucking insects. Experimental introduction of one of these viruses into the body is followed by a phase of rapid increase, during which virus circulates in the blood; at this time virus is absent from the central nervous system, and signs of illness are often trivial (Hurst 1936). Presently virus disappears from the blood, antibody appears, and the animal may thereafter remain well; it is immune to massive doses of virus given by a peripheral route, but seldom to smaller doses given directly into the brain. In a proportion of animals, a proportion varying with the identity and dose of the virus, the identity and age of the host (Sabin and Olitsky 1938), and so on, the case is different. After virus has disappeared from the blood it appears in the brain and C.S.F., and the animal develops symptoms of encephalitis. The evidence suggests that enough circulating antibody does not penetrate the blood-brain barrier to protect the nervous system, should traces of virus somehow have reached it during the phase of systemic multiplication (Hurst 1936, Schlesinger et al. 1942).

The occurrence of yet another field case suggests that infection of man is not unusual, and the probability that some cases escape involvement of the nervous system and hence pass unrecognised reinforces the suggestion. A serological survey in affected areas might yield valuable information on this point, especially since incidental observations made during the present study show that a high level of antibody to the virus persists for at least sixteen years after infection.

The course of infection with this group of pantropic viruses is such that clinical and laboratory observation from beginning to end of a case in man is rather unlikely. Hitherto diagnosis of the human malady has usually been retrospective and has depended on finding antibody to the virus in the serum of recovered patients. In the second patient investigated by Davison et al. (1948) antibody was present on the 9th day of nervous symptoms. From the experimental findings cited above it would be expected that antibody would be present at a still earlier stage, and in the blood of the present patient it was already present in good titre on the 3rd day of nervous symptoms. It follows that, when nervous symptoms have developed detectable virus must have disappeared from the blood. Experimental work offered the hope that it might still be isolated from the brain or C.S.F., and we succeeded in isolating virus from the C.S.F. even though, owing to delays in the post, four days elapsed between collection of the fluid and its inoculation into mice. At the time when the average case of human louping-ill comes under observation, therefore, it is evident that inoculation of the C.S.F. intracerebrally and intramuscularly into mice is the appropriate diagnostic procedure.

REFERENCES

Davison, G., Neubauer, C., Hurst, E. W. (1948) *Lancet*, ii, 453.
Hurst, E. W. (1936) *J. Path. Bact.* **42**, 271.
Pool, W. A., Brownlee, A., Wilson, R. D. (1930) *J. comp. Path.* **43**, 253.
Rivers, T. M., Schwentker, F. F. (1934) *J. exp. Med.* **59**, 669.
Sabin, A. B., Olitsky, P. K. (1938) *Proc. Soc. exp. Biol., N.Y.* **38**, 595.
Schlesinger, R. W., Morgan, I. M., Olitsky, P. K. (1942) *J. Amer. med. Ass.* **119**, 618.

". . . We must not enter into judgment on the patient; but we can help him to judge himself more fairly. The richest gift we can bestow upon a sick man is our unwavering friendship. When he realises that, knowing him better even than his wife does, we are nevertheless fond of him, he can take the first step towards loving and accepting himself (which is a very different matter from narcissism or even self-righteousness). From thence it is a small cry to loving and accepting his neighbours more fully: in other words, towards achieving temporarily and perhaps maintaining a better adjustment to life. The chances are that by this time we shall be as fond of him as we are of children with all their naughtiness. If we are not, and feel he's a Bad Type, it would be better to hand his case on to someone else."—"PETER QUINCE," *Brit. med. Students' J.*, Spring, 1949.

Digitized by Google

WATER-SOLUBLE VITAMIN K IN THE NEWBORN

RONALD R. GORDON
M.C., M.D. Glasg., M.R.C.P., D.C.H., D.Obst.R.C.O.G.
LATE PÆDIATRIC REGISTRAR, DEPARTMENT OF OBSTETRICS, HAMMERSMITH HOSPITAL

THE original vitamin-K analogues used for intramuscular injection were prepared as an oily solution. This often proved irritating and sometimes produced an abscess at the site of injection. Such an abscess was usually sterile, so faulty injection technique seemed an unlikely cause. Since the vitamin-K analogues themselves are not irritant, the oil in which they were dissolved must be held responsible for the abscess. To avoid this unpleasant side-effect, water-soluble analogues have now been prepared. The object of the present investigation was to discover whether this new form of vitamin-K analogue is liable to cause abscesses, and, if not, whether it is reliable in its potency, as judged by prothrombin-time estimations.

The substance was put up in 1 ml. ampoules, each containing the equivalent of 10 mg. of menaphthone (*B.P.*) in a sterile watery solution.

The subjects were normal newborn infants, none of whom showed any evidence of hæmorrhagic incidents and all of whom received the same postnatal routine attention, including being put to the breast every 3 hours, starting 12 hours after delivery.

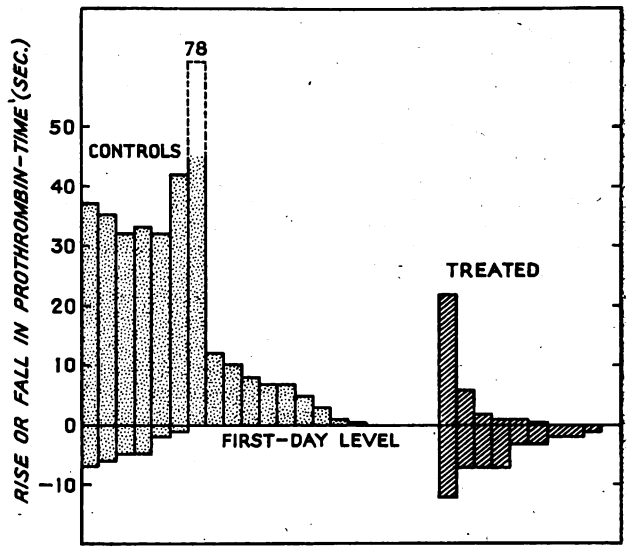
RESULTS

Abscess Formation.—A total of 52 infants received one injection of 1 ml. of the water-soluble vitamin-K analogue into the gluteal muscles. In all cases the injection was made by one of the senior nurses as part of the routine treatment of the ward. Not one infant developed an abscess.

Prothrombin-time.—Prothrombin-times were estimated on the plasma of 37 infants on the first day of life (within 24 hours of delivery) and again on the fourth day. Of these infants, 15 received 10 mg. of water-soluble vitamin-K analogue intramuscularly immediately after the first-day specimen of blood had been taken, whereas 22 controls received no vitamin-K analogue. In neither the treated nor the control group had any mother received vitamin K antenatally.

From each infant 2 ml. of blood was taken on the first and fourth days. The blood was obtained from either the external or internal jugular vein; it was then put immediately into a test-tube containing dried potassium and ammonium oxalate in the proportions recommended by Wintrobe (1946). Gentle mixing prevented clot formation. The prothrombin-times were estimated on the plasma within 2 or 3 hours of removal by Mr. L. H. Turnbull, chief technician in the clinical pathology laboratory, using the method described by Fullerton (1940). The Russell's viper venom was freshly prepared and kept in the refrigerator at 0°C until used. Each estimation was controlled by an estimation on an adult. The results, however, will be expressed in seconds rather than as an index of "normal." Mr. Turnbull was unaware which infants had received vitamin-K analogue and which were controls.

When, as here, the prothrombin-time is expressed in seconds it must be appreciated that a lengthening of the prothrombin-time indicates a fall in the prothrombin content of the plasma and vice versa. The usual course of events in the neonatal period is that the prothrombin-time is normal (18–25 sec.; Fullerton 1940) at birth, lengthens on the second, third, or fourth day, and returns to normal by the end of a week (Waddell and Guerry 1939, Quick and Grossman 1940, Brinkhous et al. 1937, Waddell and Lawson 1940, Valentine et al. 1941). If vitamin K or one of its analogues is administered either to the mother antenatally or to the infant just after birth this lengthening of the prothrombin-time does not occur (Snelling 1940, Waddell and Guerry 1939, Waddell 1942). The object of this part of the investigation, therefore, was to discover whether, in the group of infants given water-soluble vitamin-K analogue, the prothrombin-time remained the same on the fourth day as it had been on the first, and to show that the normal lengthening occurred in the control group.



Change in prothrombin-times between first and fourth days of life in 15 infants treated with water-soluble vitamin-K analogue and in 22 controls. Note: rise indicates reduction in prothrombin content of plasma.

PROTHROMBIN-TIMES IN INFANTS ON FIRST AND FOURTH DAYS OF LIFE. "TREATED" GROUP RECEIVED 10 MG. OF WATER-SOLUBLE VITAMIN-K ANALOGUE IMMEDIATELY AFTER REMOVAL OF BLOOD FOR FIRST-DAY ESTIMATION. "CONTROL" GROUP RECEIVED NO VITAMIN-K ANALOGUE

Treated group			Control group		
Case no.	Prothrombin-time (sec.)		Case no.	Prothrombin-time (sec.)	
	First day	Fourth day		First day	Fourth day
1	30	18	16	24	101
2	21	18	17	22	20
3	22	20	18	18	55
4	23	16	19	20	27
5	22	14·5	20	18	50
6	22	15	21	19	22·5
7	18·5	19·5	22	26	33
8	23	22	23	41	34·3
9	30	27·5	24	21	56
10	15	37	25	26	21
11	19	25	26	20	21
12	20	22	27	21	16·5
13	17	18	28	23	22
14	19	19	29	14	18·5
15	26	24	30	22	55
			31	20	28
			32	18	30
			33	14·5	26
			34	19	19
			35	22	16
			36	28·5	61
			37	22·5	62
Average	21·8	21·0	Average	21·8	36·1

The readings on the first and fourth days in the 15 infants of the treated group and in the 22 controls are shown in the table. It will be seen that the average reading on the first day is exactly the same in both groups—21·8 sec. On the fourth day, however, the average time of the treated group is little changed, at 21·0 sec., whereas in the control group it has lengthened to 36·1 sec. The average readings therefore indicate that water-soluble vitamin-K analogue does prevent the lengthening in prothrombin-time usual in the newborn period.

Digitized by Google

The effect of the water-soluble vitamin-K analogue in individual cases is perhaps more clearly shown in the figure. Here the base-line represents the first-day reading of each infant; lengthening or shortening of the prothrombin-time on the fourth day is represented in seconds above or below the base-line.

In the control group 15 of the 22 infants showed some lengthening of the prothrombin-time on the fourth day, and in 12 of them it lengthened by 7 sec. or more. In one it lengthened by 68 sec. and in one it remained the same. In the treated group, however, only 5 of the 15 infants showed any lengthening at all, and in only one of these was the increase more than 7 sec. In this one infant in whom the vitamin-K analogue did not appear to act its administration could not be definitely confirmed. But, even if this one case is accepted as a failure, sufficient evidence has been produced to show that the water-soluble vitamin-K analogue is effective in the great majority of cases.

DISCUSSION

This report deals solely with the non-irritancy of water-soluble vitamin-K analogue and its ability to prevent the lengthening of the prothrombin-time which usually occurs in the newborn period. It makes no contribution to the question whether vitamin K plays any part in the prevention of hæmorrhagic disease of the newborn, which seems to have been convincingly answered in the negative by Sanford et al. (1942) and Potter (1945). It does, however, show once again that very long prothrombin-times can occur without any visible hæmorrhage and helps to confirm the opinion of Capon (1942) and others that prolongation of the prothrombin-time cannot be the sole cause of hæmorrhagic disease of the newborn. Some additional factor must also be present; but, once this additional factor has come into play and the infant has started to bleed, there are few clinicians today who would not give vitamin K. It is also the practice of many, when bleeding is expected or possible, as after a difficult forceps delivery, to administer the vitamin to prevent or limit bleeding from damaged vessels. For these purposes an effective and non-irritant preparation is needed, and water-soluble vitamin-K analogue appears to satisfy both requirements.

SUMMARY

Water-soluble vitamin-K analogue, when injected intramuscularly in newborn infants, shows no tendency to cause abscesses at the site of injection.

The water-soluble analogue appears to have the same action as vitamin-K analogues in oily solution in preventing the usual fall in the prothrombin content of the plasma in the first few days of life.

The prothrombin-time of newborn infants can be greatly prolonged without any bleeding taking place.

This work was performed in the branch of the Institute of Child Health of the University of London which operates at Hammersmith Hospital. My thanks are due to Prof. Alan Moncrieff, director of the institute, for encouragement and advice; to Prof. James Young in whose department the work was performed; and to Mr. L. H. Turnbull who did most of the work. The analogue used in the investigation was kindly supplied by Messrs. Boots Pure Drug Co.

REFERENCES

Brinkhous, K. M., Smith, H. P., Warner, E. D. (1937) *Amer. J. med. Sci.* **193**, 475.
Capon, N. B. (1942) *Lancet*, **1**, 602.
Fullerton, H. W. (1940) *Ibid*, **ii**, 195.
Potter, E. L. (1945) *Amer. J. Obstet. Gynec.* **50**, 235.
Quick, A. J., Grossman, A. M. (1940) *Amer. J. med. Sci.* **199**, 1.
Sanford, H. N., Shmigelsky, I., Chapin, J. M. (1942) *J. Amer. med. Ass.* **118**, 697.
Snelling, C. E. (1940) *J. Pediat.* **17**, 615.
Valentine, E. H., Reinhold, J. G., Schneider, E. (1941) *Amer. J. med. Sci.* **202**, 359.
Waddell, W. W. jun. (1942) *J. Amer. med. Ass.* **118**, 1389.
— Guerry, D. (1939) *Ibid*, **112**, 2259.
— Lawson, G. M. (1940) *Ibid*, **115**, 1416.
Wintrobe, M. M. (1946) Clinical Hematology. 2nd ed., Philadelphia; p. 241.

Reviews of Books

Penicillin and other Antibiotics

G. W. S. ANDREWS, M.B. Lond.; J. MILLER, B.SC. Lond., assistants in the Wright-Fleming Institute of Microbiology, St. Mary's Hospital, London. London: Todd Publishing Group. 1949. Pp. 160. 7*s.* 6*d.*

THIS is one of the best short books on the subject. To the medical man who has used antibiotics it gives a lucid account of their isolation and chemical identity; to the general scientist—and even those engaged in the production of these substances—it puts their place in therapeutics into reasonable perspective. It is well documented, and the pictures, though few, really illustrate the text.

Treatise on Surgical Infections

FRANK L. MELENEY, M.D., associate professor of clinical surgery, Columbia University, New York. New York and London: Oxford University Press. 1948. Pp. 713. 63*s.*

THIS book shows how changed is the contemporary outlook of the surgeon from those of his forerunners. It emphasises the influence of biological factors on the outcome of the purely mechanical procedures of the surgeon's art. It demonstrates the futility of craftsmanship if there is craftsmanship alone. One realises that the surgeon, besides having operative skill, must be a bacteriologist, a physiologist, an immunologist, in fact a biologist in the widest sense, in order adequately and intelligently to grapple with the problems before him. Professor Meleney is as well known as a bacteriologist as a surgeon, and seems to have spent at least half his time in the laboratory. This is the trend of the training of the modern surgeon, in days when nearly all things are possible technically and nearly all techniques have been accepted and standardised in some degree. Though his book is an excellent treatise on the bacteriology of wounds, it is also more; for everything is regarded in relation to the surgeon's need to take some active steps. Then there is the whole subject of the prevention of infection, by the sterilisation of materials and of the patient—of operative-room technique, here unfortunately labelled sterile technique. The question of antiseptics is considered, and the part played by the antibiotics and by bacteriophages. The book has a good bibliography, and is a scientific and scholarly contribution to the art of surgery.

Practical Aspects of Thyroid Disease

GEORGE CRILE, jun., M.D., F.A.C.S., department of surgery, Cleveland Clinic. London and Philadelphia: W. B. Saunders. 1949. Pp. 355. 30*s.*

THIS compact and straightforward account of thyroid disease is written by a surgeon who has not neglected the purely medical and physiological aspects of his subject. Naturally enough, the surgery of toxic goitre and of malignant disease are considered in greatest detail. The difficult problem of the potential malignancy of nodular goitres is dealt with sensibly; Crile points out that there is less risk of a carcinoma arising in a nodular goitre than in a normal breast, and that the prophylactic partial thyroidectomy often advocated by surgeons is in any case inadequate. He recommends that all cases of thyrotoxicosis with nodular goitres should be treated by subtotal thyroidectomy after preparation with an antithyroid drug; those with diffuse goitres (unless the goitre is very large) should be given a long trial of antithyroid therapy in the hope of securing a permanent remission. Radio-iodine is reserved for elderly patients, or those who have developed complications after surgery or drug treatment; the small number of cases so far treated have done well. There is a full but not altogether satisfactory account of the awkward problem of subacute and chronic thyroiditis. By insisting on the existence of three wholly distinct types of thyroiditis the author finds himself left with a rather large proportion of unclassifiable cases. The technical aspects of thyroidectomy are well described, and the results of the operation are analysed in greater detail than usual. The author's ideas are rather more orthodox than those of his celebrated father, but his surgical standards are no less high.

Digitized by Google

Studies of Chronic Pyelonephritis with Special Reference to the Kidney Function

FLEMMING RAASCHOU. Copenhagen: Munksgaard. 1948. Pp. 260. Dan. kr. 20.

THIS book will interest those who use the modern clearance methods for determining kidney function. It deals in the main with the disturbances of renal functional pattern in pyelonephritis, but its particular value lies in a critical discussion of the theoretical basis of the more complicated physiological tests and their interpretation. Raaschou writes authoritatively, as one of a team which has made a special study of the modern clearance techniques. His brief consideration of the pathology of pyelonephritis is followed by the results of the various tests in this condition. He has been able to trace a broad pattern of disturbed function which is characterised by a greater diminution of tubular activity than of glomerular filtration. However, the picture is not clear-cut; and this seems largely to have been due to poor selection of cases. The series investigated includes patients who, in addition to pyelonephritis, were suffering from hydronephrosis, hypertension, diabetes, cardiac failure, and anæmia—all conditions which themselves produce disturbances in the kidney. Despite this defect, the material is well presented and is a valuable contribution to our knowledge of an important but relatively neglected subject.

Experimental Immunochemistry

ELVIN A. KABAT, PH.D., associate professor of bacteriology, College of Physicians and Surgeons, Columbia University and the Neurological Institute, New York; MANFRED M. MAYER, PH.D., associate professor of bacteriology, Johns Hopkins University, Baltimore. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 575. 45*s*.

FOR the first time the various techniques and results of workers in immunochemistry have been gathered together in an orderly way and presented conveniently in a book.

Part I deals with immunological methods for the demonstration of such substances as precipitins, agglutinins and antibodies, as well as the methodology of complement and complement fixation, anaphylaxis, and allergy. Part II covers among other things criteria of homogeneity of proteins and carbohydrates, and the effect of chemical treatment in altering immunochemical properties of proteins and polysaccharides. In part III chemical, physical, and special procedures in immunochemistry are given in practical detail, and useful chapters are included on electrophoretic analysis, ultracentrifugal analysis, and diffusion methods. Part IV describes methods of preparing individual proteins, enzymes, and polysaccharides. References to original papers amplify the text and there is a good system of cross-references.

The authors have done much to stimulate interest and encourage future progress in their subject.

Minor Surgery (3rd ed. London: H. K. Lewis. 1948. Pp. 430. 22*s*. 6*d*.).—Few changes have been necessary in this third edition of Mr. R. J. McNeill Love's deservedly popular little book, which so adequately describes the orthodox practices of minor surgery. Like all such works, it strays here and there into the major realm; but wise choice justifies the author, for these major procedures might in emergency have to be dealt with by any houseman. Full and valuable chapters on fractures and anæsthetics have been written by the author's colleagues, Mr. F. P. Fitzgerald and Dr. Donald Blatchley.

Our Plundered Planet (London: Faber & Faber. 1949. Pp. 192. 10*s*. 6*d*.).—This book by Fairfield Osborn is one of several calling attention to man's habit of wasting the resources of the world. We are as yeast plants exhausting our supply of food, and poisoning ourselves with the products of our activity. Man does not realise that nature gives no blank endorsement to the profit motive. All who care about tomorrow must remember the interdependence of all living things. Every tree felled in the U.S.A. or Australia influences the amount of food available to our descendants in the British Isles or in Tahiti. Here is a book, written by a scientist with the help and advice of numerous geographers, anthropologists, and other scientists, setting out the facts of man's exploitation of our planet, of his wasting of its substance with riotous living. It is by far the most compelling statement of the case we have seen, and should carry conviction to the stupidest prodigal son—if he will only read it.

German-English Medical Dictionary (London: H. K. Lewis. 1949. Pp. 241. 27*s*. 6*d*.).—One of the hardest tasks facing the compiler of a specialised dictionary is to decide how wide the net should be cast in gathering words for inclusion. In composing this new work, the late Dr. F. S. Schoenewald culled words and phrases from some 30,000 pages of medical publications in the English language; and, as might be expected, this diligence has resulted in a collection that really does cater for the medical translator. The author has taken unusual pains to explain the different shades of meaning that may be applied to a single German word. Thus we are reminded that "Blatt" may be used to denote a *blade* of forceps (or a fern), a *leaf* of a book (or a tree), or a *sheet* of epithelium. The printing, paper, and binding are pleasingly reminiscent of more opulent days.

A Method of Anatomy (4th ed. London: Baillière, Tindall, and Cox. 1948. Pp. 852. 38*s*. 6*d*.).—Departing from the traditional method, Prof. J. C. Boileau Grant, of Toronto, has endeavoured to present anatomy rationally in a manner readily understood and remembered by students. Structures are related to each other and to functional processes, and the lesson is driven home by appropriate references to developmental and comparative anatomy. The result is a clear, stimulating text which avoids tedious and unnecessary details. In this edition there are revisions and additions. The author draws new analogies with easily understood mechanical principles and makes further excursions into embryology and comparative anatomy to illustrate and explain the structure of the body. Some 68 additional pictures account for the growth of the book. They illustrate, among other things, Professor Grant's gift of comparing structures with objects of common experience—for example, the coracoid process with the crooked index finger. Many of the original diagrams have been redrawn and relabelled; every diagram is relevant, and so simple that even the least artistic could copy it. The descriptive methods used would apply particularly well to the central nervous system, which unfortunately is omitted. Perhaps the author can be induced to put it into the next edition, thus making his book a complete guide to topographical anatomy. It can be recommended to the student, whatever stage he has reached in his studies—not to replace the encyclopædic reference books, but as a "working instrument" to an intelligent and thorough understanding of the normal body.

Science for Peace and Socialism (London: Birch Books. 1949. Pp. 86. 2*s*. 6*d*.).—This book, by Prof. J. D. Bernal, F.R.S., and Mr. Maurice Cornforth, summarises the thesis underlying several recent and projected conferences, whose slogan is provided by its title. Professor Bernal deals with the effects of capitalism and Anglo-Saxon imperialism on science and its prospects, Mr. Cornforth with the corruption of scientific philosophy by its bourgeois and reactionary exponents. In a less biased and shortsighted presentation, Professor Bernal's arguments would carry great weight: the Communists are not alone in their concern at the growth of military secrecy in science, or in recognising the militarisation of the West. A large proportion of scientific readers, however, would level equally serious criticism at both protagonists in the present East-West conflict; and some (in view of modern weapons and of the crises which exist in nutrition and in mental health throughout the civilised world) would dissociate themselves from the support of any military action, for or against either side. Mr. Cornforth carries less conviction than his fellow author: the firmest believers with him in the value of scientific materialism might find his ideological denunciations of post-Einsteinian cosmology highly uncongenial, suggesting as they do the very type of irrationalism and subjectivity which he deplores. It is impossible to accept his thesis as a remedy for the growth of mystical at the expense of scientific attitudes—it contains in itself too strong an element of political mysticism. The social studies which he suspects of being instruments of the capitalist system provide a more rational assessment both of the pretensions of the West and of those of Russia, and are severer and more constructive critics of both, in that they base their conclusions on investigation rather than the fundamentalism which inspires this book.

Digitized by Google

THE LANCET

LONDON: SATURDAY, APRIL 23, 1949

Achievements with Chloromycetin

Two recent communications emphasise the importance of the antibiotic chloramphenicol, better known as 'Chloromycetin.' In the first, a paper read before the American Chemical Society on March 29, Messrs. Parke, Davis & Co., of Detroit, gave a detailed account of its synthesis: we published their formula on April 2, and it has since been discussed by RAISTRICK.[1] The second, a report [2] from the Army Medical Department Research and Graduate School, Washington, D.C., and the Institute for Medical Research, Kuala Lumpur, Malaya, shows that the synthetic drug reproduces in their entirety the remarkable successes in the treatment of scrub-typhus which have previously been attained with chloromycetin prepared by the fermentation process.[3] Of such significance are these achievements—to the clinician, experimental pathologist, epidemiologist, and biochemist, and also to the civilian and soldier serving in the Far East—that the phases of the investigations deserve recapitulation.

The first phase began when PAUL R. BURKHOLDER, a botanist of Yale University, studied a soil actinomycete recovered during 1947 from a soil sample taken from a mulched field in Venezuela. His preliminary tests showed that it had antibacterial activity, and he passed it on to the research division of Parke, Davis. In the second phase, EHRLICH and his colleagues [4] obtained from the organism a highly purified crystalline derivative, which proved active against *Rickettsia prowazeki*, the semi-virus responsible for louse-borne typhus. The crystalline product derived from the mould (now named chloromycetin) was thereupon submitted to Dr. JOSEPH E. SMADEL, director of the department of virus and rickettsial diseases at the Army Medical Research and Graduate School, who undertook more extended tests in vivo. In this third phase he [5] showed that in embryonated eggs and in laboratory mice, infected severally by appropriate routes with the causal rickettsia of scrub-typhus, louse-borne typhus, murine typhus, Rocky Mountain spotted fever, rickettsialpox, and two strains of psittacosis virus, chloromycetin was very effective. The drug was active by mouth, and its toxicity was very low. In its fourth phase therefore the investigation moved to the hospital ward, and in a short visit to Mexico in January, 1948, SMADEL and his colleagues [6] treated a small group of patients suffering from louse-borne typhus, with encouraging results.

Scrub-typhus next claimed attention. During the war this mite-borne jungle form of typhus fever had caused some 25,000 casualties among British and American troops in the South-East Asia command and the South-West Pacific theatre, with an approximate death-rate of 10%, and an invaliding-rate of another 25%. After the war, British and American forces were still on garrison duties in those areas, and the disease also remained a constant menace to the planting communities of Malaya and adjacent territories. At Kuala Lumpur was a modern laboratory, the Institute for Medical Research, at which much intensive investigation of the disease had been carried out by the late Dr. WILLIAM FLETCHER and later by Dr. RAYMOND LEWTHWAITE, the present director of the institute, and Dr. S. R. SAVOOR. When, therefore, in November, 1947, the commandant of the Army Medical Department Research and Graduate School inquired whether a U.S. Army research unit might have the opportunity to collaborate with the staff of the institute in trials of chloromycetin, at that time barely known, the offer was warmly welcomed by Dr. LEWTHWAITE and by the government of Malaya. In March, 1948, the unit arrived by air, complete to the last jeep, bringing with it the world supply of the fermentation drug (1 lb.)—a modern argosy that was to prove of profound import to Malaya and adjacent countries. With five members, each of high calibre, the unit comprised two virus workers, a physician, and two experienced entomologists and epidemiologists—namely, Dr. SMADEL, Dr. H. L. LEY, Dr. T. E. WOODWARD, Colonel C. B. PHILIP, and Major R. TRAUB.

Thenceforward events moved with dramatic speed and success. Within 24 hours of the unit's arrival at the institute, two soldiers, infected with scrub-typhus during training, were treated with chloromycetin of the fermentation type, by the oral route; 48 hours later, at a time when increasing fever and toxicity would ordinarily have been expected, the temperature was normal and toxicity had vanished. Favoured by an outbreak of the disease on a neighbouring rubber estate, confirmation was rapidly forthcoming; and in cases treated up to the 9th day of this 15-day febrile disease chloromycetin proved infallible. With this bastion firmly established, new lines of investigation, hitherto denied, became possible. Directed by Dr. SMADEL, the study of the chemoprophylactic potentialities of the drug was begun; for it was now possible deliberately to expose human volunteers in known infested areas of countryside, to note infection-rates and early clinical features, and to treat at will. In this the investigators were much aided by the presence at the institute of a unit comprising Dr. J. R. AUDY, Mr. J. L. HARRISON, and Mr. K. L. COCKINGS, sponsored by the Colonial Medical Research Committee, and engaged on a long-term fundamental inquiry into the ecology of scrub-typhus.

1. Raistrick, H. *Nature, Lond.* April 9, p. 553.
2. Smadel, J. E., Jackson, E. B., Ley, H. L., Lewthwaite, R. *Proc. Soc. exp. Biol. Med.* 1949, **70**, 191.
3. Smadel, J. E., Woodward, T. E., Ley, H. L., Philip, C. B., Traub, R., Lewthwaite, R., Savoor, S. R. *Science*, 1948, **108**, 160.
4. Ehrlich, J., Bartz, Q. R., Smith, R. M., Joslyn, D. A., Burkholder, P. R. *Ibid*, 1947, **106**, 417.
5. Smadel, J. E., Jackson, E. B. *Ibid*, p. 418.
6. Smadel, J. E., Leon, A. P., Ley, H. L., Varela, G. *Proc. Soc. exp. Biol. Med.* 1948, **68**, 12.

Digitized by Google

A new observation of great potential importance was made. Among the cases treated with the drug were several febrile patients who did not conform to the early clinical syndrome of scrub-typhus, and who, as expected, proved by laboratory tests to have typhoid (enteric) fever. A preliminary report on the first ten cases of typhoid treated with chloromycetin has already been published,[7] and further information should soon be forthcoming. In brief it may be said that improvement of the general condition, and lessened toxicity, usually became apparent within 24 hours of the beginning of treatment; the temperature fell to permanent normal levels within four days; and though occasionally there were relapses, these responded promptly to a second course of the drug.

Last July, after encouraging in-vivo tests of the new synthetic chloromycetin in Dr. SMADEL's laboratory in Washington, all that remained of this synthetic drug, barely enough for two human cases of scrub-typhus, was sent to Malaya for trial in man. Two Gurkha soldiers, infected during the jungle war against bandits, were selected: in one the infection was very severe; in the other it was moderate. They were treated respectively on the 5th and 6th days of the febrile reaction. In both the temperature reached normal within 48 hours and remained so; toxicity vanished and convalescence was uneventful. Since then the work in Kuala Lumpur has continued and the range of diseases investigated has been enlarged. Attempts are being made to establish a chemoprophylactic scheme of dosage, with its obvious importance to troops, planters, survey parties, forest officials, and the like. Alternative dosages aiming at simplification are under trial. A number of detailed reports are in the press, and we must not anticipate their conclusions.

The above is but a brief narrative of events that have culminated in several unique findings. A much-dreaded disease, scrub-typhus, has been successfully treated by oral administration of an antibiotic prepared from a mould by fermentation methods, and later by the same antibiotic prepared synthetically. Typhoid fever, for which we have hitherto had no satisfactory remedy, has responded to chloromycetin of the fermentation type. The limits of the drug's action have not yet been explored, but the director of Messrs. Parke, Davis's department of clinical investigation is quoted [8] as saying that it has been used with great success in primary atypical pneumonia, and that it is expected to be valuable against whooping-cough. Undulant fever, lymphogranuloma inguinale, urinary infections, and bacillary dysentery are among other conditions mentioned. But beyond all this there are the implications of successful synthesis of an antibiotic. The search for synthetic closely related antibiotics will be intensified, in the hope that the spectrum of diseases affected by this class of drugs will be widened. We must hope that reduced costs, approximating perhaps to those of the sulphonamides, will gradually free this and other such antibiotics from the restriction of use imposed by the expense of fermentation methods of preparation.

7. Woodward, T. E., Smadel, J. E., Ley, H. L., Green, R., Mankikar, D.S. *Ann. Intern. Med.* 1948, **29**, 131.
8. *New York Times*, March 27.

The Elderly Primigravida

To the woman approaching or past the forty mark a first pregnancy may well cause misgiving, for she knows that considerable social and domestic adjustment will be required of her; and her adaptability is already on the wane. Some are indignant at having "fallen" at a time when—like Abraham's wife, Sarah, who laughed—they have begun to feel secure. To others, looking back on long years of involuntary sterility, the gamble with hope may appear desperate indeed. All, moreover, are versed in the obstetrical adventures of talkative friends. This emotional background profoundly influences pregnancy, labour, and lactation. Emotion also colours the medical attendant's judgment, for he is keenly aware of the woman's limited obstetric future and the unique importance of the fœtus; and he would therefore do well to arm himself with a balanced view of the risks to mother and child.

Pregnancies in 1000 women over forty have been reviewed by DAVIS and SESKI,[1] who found that of the 168 primigravidæ in this group only 16% had spontaneous deliveries; 46% required forceps delivery, and 31% were delivered by cæsarean section. There was a maternal mortality of 1·2%, and a combined fœtal mortality (including both primigravidæ and multiparæ) of about 10%. By contrast, BROMBERGYA and BRZEZINSKI [2] reported from Jerusalem a smaller series of 67 cases where spontaneous deliveries took place in 71% and cæsarean section was performed in only 1·5%; the maternal mortality was nil, and the combined fœtal mortality 7·2%.

A more radical trend was detectable in the figures recorded by DUNCAN and GIBSON,[3] in Canada; they noted a rise in the cæsarean-section rate from 15% in women between thirty-five and forty to 36% in those over forty. Under modern conditions cæsarean section is a fairly safe operation, but it remains an unnatural insult to the peritoneal cavity and the abdominal parietes. With increasing maternal age there is an unfortunately growing readiness to undertake this operation; too often pessimism about the outcome of labour is allowed to obtrude. Apprehension, it is true, is seldom felt for the elderly multipara; with her, cæsarean section does not loom upon the therapeutic horizon until some gross complication supervenes. But multiparity is not necessarily an advantage: the multipara is often a tired woman, and previous childbirth may have impoverished her blood, endowed her with recurrent urinary infection, ruined her teeth, afflicted her with hæmorrhoids and varicose veins, accelerated the onset of hypertension, and played havoc with her abdominal wall and sacro-iliac joints. Many years ago BETHEL SOLOMONS drew attention to the "dangerous multipara" and pointed out the increasing risks in parity beyond the fifth from such factors as the pendulous belly with its effects on presentation, and the greater liability to placenta prævia, adherent placenta, uterine rupture, and similar dramatic incidents. The elderly primigravida has less obvious handicaps; the chief are a more rigid perineum and uncertain expulsive powers in labour, aggravated undoubtedly by anxiety and

1. Davis, M. E., Seski, A. *Surg. Gynec. Obstet.* 1948, **87**, 145.
2. Brombergya, Y. M., Brzezinski, A. *J. Obstet. Gynæc.* 1942, **49**, 672.
3. Duncan, J. W., Gibson, W. E. *Canad. med. Ass. J.* 1940, **42**, 240.

Digitized by Google

possibly by fear. Labour may certainly be prolonged. VIOLET SPILLER,[4] analysing the cases of 1400 primiparæ at the Royal Free Hospital, established a low but definite positive correlation between age and the duration of labour; and the belief is widely held—and supported by the observations of DUNCAN and GIBSON—that the longer the preceding period of sterility, the greater is the chance that labour will be complicated by inertia. Furthermore, the elderly primigravida has a less certain prospect of establishing and maintaining satisfactory lactation. On the other side of the balance, she scores heavily over the multipara in the matter of postpartum hæmorrhage; DAVIS and SESKI quote a 3% rate, compared with 7% in multiparæ. Furthermore, the prematurity-rate in primigravidæ is certainly not nearly as high as the 9% figure ascribed by these workers to elderly multiparæ. Pre-eclampsia is somewhat more common in primigravidæ, but at least it is not—in the nature of things—recurrent; and a first attack is less dangerous than a second or third. In the two classes the chances of fœtal abnormality are about equal and are materially higher than in younger women. BARRY,[5] for instance, showed that mongolism was related to increasing maternal age, which was also held to predispose to psychosis in the offspring.

With pregnancy in women who are past their first youth an especially careful watch has to be kept for hypertension and renal disorder; less commonly fibroids, and other disabilities which crop up as milestones on the road to the grave, have a more or less direct bearing on the outcome. Hence in giving a reassuring answer to the question "Am I too old?" there is occasion for vigilance. But there is also much from which to draw comfort.

Lead and the Red Cells

THE association of lead poisoning with punctate basophilia of the red blood-cells has been recognised for fifty years. With punctate basophilia the red cells look as if they were stippled with black dots, and this stippling is used as a measure of intoxication in lead workers; the presence of more than 1000 stippled cells per c.mm. is a signal that lead intoxication may be present. If poisoning is severe, actual anæmia occurs; and this anæmia is often said to be hæmolytic because of the presence, among other signs, of persistent reticulocytosis. Many workers have tried to find out why stippling appears and how it is connected with the anæmia of lead poisoning. Some years ago KEY[6] showed that the basophilic material of the stippling is not derived from nuclear material but is formed in the cytoplasm. AUB and his co-workers[7] thought that the effect of lead was to make the surface of the red cells inelastic and brittle, so that they were more easily destroyed and a hæmolytic type of anæmia appeared. This hæmolytic theory held the field for a long time. Eventually studies of porphyrin metabolism suggested that lead acted on red cells by interfering with hæmoglobin formation; KENCH, GILLAM, and LANE[8] showed that in lead intoxication there is restricted formation of protoporphyrin—a vital stage in the development of the pigment portion of hæmoglobin. This supported the theory that dyshæmopoiesis, and not hæmolysis, was the important change in lead intoxication.

MCFADZEAN and DAVIS[9] seem to have reconciled the two theories. They examined bone-marrow, obtained by biopsy and studied by smear techniques, from lead workers, and from guineapigs subjected to lead intoxication. They found stippling in the normoblasts, but only in those normoblasts that showed hæmoglobin formation—the polychromatic stages included. There were more stippled cells—both normoblasts and erythrocytes—in the bone-marrow smears than in the peripheral blood. Special staining showed that a varying proportion of the basophilic granules gave a positive iron reaction; and again there were more of these cells in the marrow than in the blood. These findings are remarkably similar to those recorded by the same authors[10] in some patients with acquired hæmolytic anæmia—patients whose red cells contained the so-called "Pappenheim bodies," which gave a positive iron reaction in the peripheral blood and in the marrow. When splenectomy was performed on these patients, the proportion of red blood-cells containing Pappenheim bodies was greatly increased. MCFADZEAN and DAVIS therefore removed the spleens of some of their guineapigs subjected to experimental lead poisoning; and the results were illuminating. Two groups of guineapigs, one normal and the other without spleens, were given daily doses of a lead salt; with the onset of intoxication and the appearance of stippled cells in the blood, the proportion of these cells rose to 40% in the splenectomised animals compared with a maximum of 7·5% in the controls. When the lead was stopped, stippled cells persisted longer in the blood of the splenectomised animals than in the controls; furthermore, the splenectomised animals showed little anæmia whereas in the controls anæmia was definite. In a second experiment, daily doses of lead were given to a group of guineapigs until stippled cells appeared in the peripheral blood and anæmia developed. Half the animals then had their spleens removed; the stippled cells in the blood of these animals rose rapidly to 40–50%, whereas in the controls the level remained at 2·5–7·5%. In the splenectomised animals stippled cells were more numerous than reticulocytes; in the controls this relation was reversed. There were also qualitative differences in the stippling; in the splenectomised animals most of the basophilic granules gave a positive iron reaction, whereas in the controls only a minority gave this reaction. MCFADZEAN and DAVIS conclude that lead does act primarily by disturbing hæmoglobin formation; instead of becoming fully converted into hæmoglobin, basophilic substance persists in a granular form associated with demonstrable iron; the iron in the hæmoglobin molecule will not, of course, give "free" iron reactions. When red blood-cells containing these iron-positive granules are released into the circulation, they are destroyed in the spleen much more rapidly than cells containing no granules, or only few. Consequently a truly hæmolytic anæmia appears.

4. Spiller, V. *Lancet*, 1939, ii, 733.
5. Barry, H. jun. *Arch. Neurol. Psychiat., Chicago*, 1945, **54**, 186.
6. Key, J. A. *Arch. intern. Med.* 1921, **28**, 511.
7. Aub, J. C., Fairhall, L. T., Minot, A. S., Reznikoff, P. *Medicine, Baltimore*, 1925, **4**, 1.
8. Kench, J. E., Gillam, A. E., Lane, R. E. *Biochem. J.* 1942, **36**, 384.
9. McFadzean, A. J. S., Davis, L. J. *Quart. J. Med.* 1949, **18**, 57.
10. McFadzean, A. J. S., Davis, L. J. *Glasg. med. J.* 1947, **28**, 237; see *Lancet*, 1947, ii, 840.

Digitized by Google

Thus the seemingly opposed schools are united. But, though the explanation is ingenious, the evidence that hæmoglobin formation is involved is likely to be criticised in view of evidence that the basophilic substance of erythroblasts is a ribonucleic acid.[10 11] Furthermore, the explanation of one set of facts only raises new questions. Here is a hæmolytic anæmia caused by toxic interference with the proper development of the red blood-cells. In how many other anæmias with a hæmolytic picture is there a toxic cause, and in how many are we chasing a will o' the wisp when looking for hæmolysins?

Annotations

THE NURSES' BILL

NEW Bills, like chestnut buds, are packed with promise but a bit sticky to handle. Those who have had the welfare of nursing at heart during this luckless century will be delighted with many of the provisions in the Nurses' Bill; but they may also suspect that in some ways it is a little backward for the season we have now reached.

The proposal that the finance of nurse training should be separated as far as possible from that of hospitals will get general support. The plan for reconstituting the General Nursing Council also promises well. Of the 34 members, 17 will be nurses elected by the profession, 14 of them being on the general part of the register, 2 being mental nurses, and 1 a sick-children's nurse. Of the 14 general nurses, 1 is to be elected for each of 14 geographical areas into which the Minister will divide England and Wales, and they must all, at the time of election, be engaged in nursing in the areas for which they are elected. This is a good safeguard against the appointment of those whose experience of nursing conditions is no longer first-hand. The general nurses are to be elected by nurses on the general part of the register, the mental nurses by mental nurses, the children's nurse by children's nurses; this is reasonable enough except that it seems, under this ruling, that fever nurses and nurses of mental defectives will be disfranchised. The Minister of Health will have the power to appoint 12 members of the council, of whom 2 will be registered nurses employed by local authorities, 2 will be teachers of nursing, 1 will be a male nurse, and 1 a ward sister in a training hospital. The qualifications of the remaining 6 members to be appointed by the Minister are not specified. Of the remaining 5 members of the council, 3 are to be appointed by the Minister of Education; and 2 by the Privy Council, 1 of whom is to represent the universities. This gives a council composed half of elected nurses, representing every area of the country; and including, besides, 6 appointed nurses, 5 members with an educational background, and 6 members without prescribed qualifications who may well bring into these professional deliberations a breath from the workaday world. A mental nurses' committee of the council is also to be formed—a welcome advance.

The Bill also proposes that regional nurse-training committees should be set up to advise and assist the G.N.C. and the training institutions on everything connected with the training of nurses, and to allocate the funds provided for training (by the Exchequer through the G.N.C.) to the various institutions. These committees will have the direct duty of improving methods of training, and promoting research and investigation into training methods. Live bodies of this kind have long been needed to overcome local apathy and bring backward areas up to—if possible beyond—the standards of the best. Moreover, the Bill actively encourages the reconstituted G.N.C. to experiment in methods of training. No differences in the present training, or its length, are directly proposed, but the council are at liberty to give other schemes of training a trial; and while any such scheme is in operation the student nurses taking it will be entitled, on passing the examinations specified in the scheme, to be admitted to the register, or (if the scheme applies to assistant nurses) to the roll. Some may feel that the G.N.C. will hardly be enticed into violent action by the mere permission to experiment, and that some further encouragement will probably be needed as the years go by. But at least the newly constituted body, which may well be more dynamic, would start without legal restrictions on any reforms it contemplated.

11. *Lancet*, 1948, i, 797.

A DEATH FROM DICOUMAROL

AT Battersea an inquest has been held on a woman who died from internal hæmorrhage due to dicoumarol, which had been given for thrombosis in the leg veins. The doctor is reported [1] to have said that he gave the dose recommended in the manufacturer's literature; he confessed his ignorance of the dangerous properties of dicoumarol, and complained that these were not mentioned in the instructions for use. The coroner, recording a verdict of death from misadventure, criticised the manufacturers for not making clear the dangers of this substance.

Ever since 1942, when dicoumarol was introduced as an anticoagulant, the dangers of overdosage have been fully realised by those who have worked much with the drug. Dicoumarol acts by reducing the prothrombin content of the blood, and the aim of treatment is to reduce the prothrombin concentration to below 30%, but to not less than 10%, of normal. At this level the coagulability of the blood is significantly decreased; and below 10% there is grave danger of serious hæmorrhage that may be difficult to stop. If we could give a certain dose of dicoumarol and know that it would reduce the prothrombin concentration by so much, treatment would be simple. Unfortunately, the reduction in prothrombin concentration brought about in different persons by a given dose of dicoumarol varies greatly.[2] Consequently, for complete safety, daily estimations of prothrombin concentration[3] are required. Moreover, we now know that methods of estimating prothrombin which employ Russell viper venom as a thromboplastin [4] are liable to serious inaccuracies. Ball and Hughes [5] have lately described a technique which they regard as accurate. It is essentially similar to Quick's classical one-stage method, but uses a preparation of thromboplastin made from human brain instead of from rabbit brain.

Whether receiving initial heparin or not, the patient is given 300 mg. of dicoumarol by mouth on the first day, and 200 mg. on the second day; further doses depend on the prothrombin concentration, which is estimated every day before any dicoumarol is given; the daily dose varies between 100 and 200 mg., provided the prothrombin concentration is over 20%. In a case of venous thrombosis, the prothrombin concentration is usually kept low by dicoumarol administration for 7–10 days; then no more is given, for the effect of the drug continues for some days longer. This sort of control calls for a special "anticoagulant control team"; it cannot even be undertaken properly by individual units. Suitable care of this sort is rewarding; of 74 patients with deep thromboses treated by Ball and Hughes,

1. *Evening Standard*, April 4.
2. *Lancet*, 1944, ii, 412.
3. *Ibid.*, 1948, i, 601.
4. Fullerton, H. W. *Ibid*, 1940, ii, 195. Witts, L. J., Hopson, F. C. G. *Ibid*, p. 247.
5. Ball, K. P., Hughes, H. O. *Brit. med. J.*, April 2, p. 560.

Digitized by Google

only 5 relapsed while on treatment and 4 after treatment had stopped, and satisfactory results were also obtained in pulmonary embolism. They had some hæmorrhagic incidents, mostly among early cases when they were using a viper-venom method; none was fatal.

Whether manufacturers should emphasise in their literature the dangers of their products is a matter of commercial ethics; some do give excellent accounts of methods of control and of contra-indications, but others do not. Despite all that has been said and written to the contrary, folic acid is still being advertised for the treatment of pernicious anæmia; and the pamphlets that accompany active hormone preparations are often not very emphatic about the dangers of overdosage. Yet to place responsibility for proper use on the salesman is hardly fair; for he is rarely a medical man, and commonly he has little deep knowledge of the properties of his products. The responsibility must be the doctor's, but there should also be some method of marking plainly drugs that are only suitable for hospital use; nitrogen mustard—a most dangerous drug in inexpert hands—is on sale to any doctor.

IRREGULAR DISCHARGE FROM SANATORIA

In the United States, the proportion of irregular discharges of tuberculous patients from sanatoria has caused much concern to the Veterans Administration; their research division has analysed exhaustively data gathered by the social service staff in an effort to find a reason for so high a figure as 54·4% in 1946–47 leaving prematurely, and against medical advice.[1] The rate was 72·5% in 1945. Corresponding figures in Great Britain vary considerably, from 5% in Manchester and 8% in Lancashire, to an average of 24% for a group of Welsh hospitals. These figures for Great Britain are taken from independent reports of local authorities, and refer to adult men and women—not solely, like the United States figures, to men who were in the Forces.

"Emotional and psychic factors were found to have an effective contributory force in most cases of the development of tuberculosis"; indeed anxiety and fear were very commonly expressed in the behaviour of these tuberculous patients. Many veterans dislike hospital life, detecting in it memories of military discipline. A little less than half the irregular discharges were found to be due to events and conditions outside the hospital. Remedial measures suggested are intensive social case-work with the patient and family before and during the patient's stay in hospital; psychiatric treatment, and instruction to the staff on the emotional and psychic components and concomitants of tuberculosis; more individual consideration or treatment by the medical staff; and more careful and considerate application of hospital rules. The tuberculous patient needs help and support to withstand the emotional strains which sanatorium treatment produces.

"Irregular discharge" can be interpreted in more than one way; a tighter definition is needed before close comparisons can be made with figures in this country. Furthermore, we have no recent survey to compare with this study by the Veterans Association. Our rate of irregular discharge is undoubtedly much lower, however, and this is most likely due to such factors as the effective advice, supervision, and education given by the chest physician and health visitor; greater confidence of the patient in his treatment, in which he is supported by the family; and economic help for the patient and family in our "welfare State." It may be, too, that we are as a people more persuasible than Americans, less independent in behaviour, and more inclined to give the doctor credit for knowing what he is about. There is scope, however, for research in Britain to ascertain accurately the irregular-discharge rate, matching the result of investigations elsewhere factor by factor. Here is a chance for one or more of our new regional hospital boards to investigate a factor which affects greatly our success in preventing and treating tuberculosis.

1. Irregular Discharge (Veterans Administration pamphlet 10–27). Washington, D.C.: U.S. Government Printing Office. 20 cents.

ENCEPHALOPATHY FOLLOWING PERTUSSIS VACCINE

Since 1933 there have been several reports of convulsive attacks, and even of fatal encephalopathy, following the prophylactic use of pertussis vaccine; but they have attracted little attention. The publication by Byers and Moll[1] of a series of 15 such cases from the Children's Hospital in Boston airs a problem which is the more disturbing in that it remains unsolved. The incidence of the cases was spread over a period of eight years; they were geographically dispersed, and the products of eight different manufacturers were used. The age of the infants varied from five to eighteen months, and 12 were males. Convulsions followed the injection after an interval varying from twenty minutes to seventy-two hours, and in 6 of the cases the first dose precipitated the attack. Sensitisation therefore appears unlikely. The convulsions were followed by coma in some, or hemiplegia and exaggerated tendon-reflexes. The cerebrospinal fluid showed a slight excess both of protein and of mononuclear cells. An infective agent therefore appears improbable. The illness lasted from thirty-six hours to ten days, and the most sinister feature has been the persistence, in all but 1 infant of neurological residua of different kinds. Thus about half have shown retardation of mental development, 3 being grossly defective; 2 became blind; 3 continued to have convulsions; and 5 were hemiplegic. In 2 cases the infant later died of pneumonia, and at necropsy on one of these, performed at a State institution, the brain was said to show diffuse atrophy and gliosis. The demonstration of ventricular dilatation by means of pneumoencephalography in 6 out of 8 of the others certainly indicates a similar order of structural change.

But the fundamental pathology of this encephalopathy remains obscure. The scattering of the cases in space and time seems to exonerate the preparations used for the injections, and suggests rather that the infants were in some way constitutionally vulnerable. And this suggestion finds some support in the record of epilepsy, hydrocephalus, or convulsions in the siblings of 3 cases of the series. It is of interest that Byers and Moll report, within the same period, the admission to the Children's Hospital of 26 infants showing encephalopathy during an attack of pertussis, of whom 7 died. It cannot therefore be said that the casualties arising from prophylactic treatment are of an order that outweighs its advantages.

1. Byers, R. K., Moll, F. C. *Pediatrics*, 1948, **1**, 437.

AN INCONCLUSIVE INQUIRY

In the autumn of 1946 a group of workers appointed by the American Trudeau Society set out to investigate several questions surrounding the use of streptomycin in tuberculosis. Among the points they sought to determine were: (1) the types of pulmonary tuberculosis most likely to benefit from this drug; (2) the most satisfactory methods and frequency of treatment, the optimum daily dosage, and the optimum duration of treatment; and (3) the most timely integration of streptomycin with other therapeutic procedures. Their report is to be published in full as a book. Meanwhile a summary[2] records that altogether 566 patients were treated under this scheme and analyses the findings in 332 with pulmonary tuberculosis who were observed for at least

2. Riggins, H. M., Hinshaw, H. C. *Amer. Rev. Tuberc.* 1949, **59**, 140.

Digitized by Google

90 days from the start of treatment. Apparently pulmonary tuberculosis of all types was included; 17 had minimal, 118 moderately advanced, and 197 far advanced disease. There were four main treatment groups: Group A were treated for periods ranging from 30 to 89 days with doses varying between 0·5 and 1·4 g. streptomycin daily; group B were treated for a similar period with 1·5–3·0 g. daily; group C were treated for 90 days or more with 0·5–1·4 g. daily; and group D were treated for a similar period with 1·5–3·0 g. daily. The size of these groups was unequal, with 124 patients in the first group, and 46, 89, and 73 in the other three. The distribution of lesions in the groups was also unequal: group A included less than 40% of patients with an acute type of disease, and group B over 60%; in up to 10% the type of disease was not stated. Moreover, each of the eight clinical investigators seems to have had the right to choose one or several of the treatment groups as he pleased. The duration of observation in the four groups was 182, 234, 264, and 294 days.

The results have been analysed on the basis of radiological and other assessments made by the clinicians in charge of the patients; and the statistics were compiled centrally by the staff of the U.S. Public Health Service. The main analysis shows greatest clinical and radiological improvement in the groups receiving the largest dosage. Unfortunately, however, the multiple inequalities between the groups are so important that it seems, on reading the summaried report, that no conclusion is justified.

The analysis is followed by a long chapter of discussion at a high level, of the order one has come to expect from the authors of this report. They make wise general evaluations of the scope of streptomycin therapy which should be very useful to clinicians handling this drug. They also make reservations concerning the results of the analysis; but these scarcely redeem the fact that a project involving considerable effort by experienced clinicians has yielded little save impressions. These impressions would have been as easily gained without an organised trial. The value of a planned investigation depends on the quality of the planning.

PSYCHOMOTOR EPILEPSY

THE psychomotor attack is all too often wrongly diagnosed in practice. The mental symptoms may be interpreted as evidences of hysteria or of a schizoid psychosis, or, if the underlying epileptic basis is perceived, the attacks may be regarded as a form of petit mal. (The latter term, indeed, is commonly used to cover any and every epileptic manifestation except the complete major fit.)

An electro-encephalographic approach to the study of these attacks is reported by Gibbs et al.[1] The Boston school were the first to claim a typical E.E.G. picture for this type of fit, and their paper attempts a more elaborate definition of the psychomotor type of discharge. Verbal description is, however, at best clumsy, and recognition of this type of dysrhythmia in its many variations can, they say, be attained only by experience. Of 300 cases selected solely on the basis of a typical E.E.G. abnormality, over 90% proved to have clinical psychomotor attacks characterised by amnesia, confusion, and some retention of consciousness, with purposeful, but poorly coördinated, movements, usually simple and repetitive. (Unfortunately it is not stated what proportion of patients with clinical attacks do not show the appropriate E.E.G. abnormality.) In inter-seizure periods severe personality disorders were common, and some of the patients were classified as psychotic. Hypersomnolence, irrespective of medication, was often present. In the E.E.G. the disturbance was found to arise in the anterior temporal area—sometimes on the right side, sometimes on the left, and sometimes on both—and the focus showed up best during sleep, natural or induced. Only one patient in seven had neurological signs or aura suggesting involvement of the temporal lobe, and a history of head injury in the temporal region was rarely obtained. A history of epilepsy in near relatives, on the other hand, was noted in 4·5% of the cases—an incidence higher than that found by Lennox et al.[2] in idiopathic epilepsy generally. The important deduction is made that this type of focus is heritable. Personality disorders are much commoner in association with psychomotor attacks than with grand mal or petit mal, and it seems reasonable therefore to attribute much of the so called "epileptic personality" to disturbances in the anterior temporal area.

An interesting confirmation of this has been provided by Belinson[3] who found, by E.E.G. standards, psychomotor manifestations more than three times as often in epileptics living in institutions than in epileptics living in the community. The associated behaviour difficulties, rather than the number and severity of fits or the degree of retardation, were no doubt the main cause for admission to an institution. This and other distinctive features in Belinson's E.E.G. records of epileptic patients in institutions, emphasise once again the necessity of defining as exactly as possible, the selective factors at work in determining the composition of any group of patients to be submitted to investigation.

COÖRDINATING MEDICAL CONGRESSES

A Council for the Coördination of Medical Science Congresses was formed at a conference of non-governmental organisations held in Brussels this month under the joint ægis of W.H.O. and UNESCO. The council, whose permanent headquarters are to be in Brussels, will suggest appropriate places and dates for medical congresses, and enable scientists in related branches to attend particular gatherings without duplication and unnecessary expense; subsidies may be granted to those wishing to attend. The organisers hope that the establishment of the council will cause future congresses to be held in parts of the world which have hitherto been neglected as meeting-places. The council also proposes to study conference techniques, and to help congresses by offering such services as translation, interpretation, and record-making, and by publishing proceedings. The work is to be financed through dues contributed by non-governmental organisations, while W.H.O. and UNESCO will contribute the cost of various services. The chairman of the executive committee is Prof. Joseph Maisin, director of the Cancer Institute of Belgium.

THIS week the President of the United States introduces to Congress his National Health Bill. It will offer complete medical care for about 85 million wage-earners, and will tax them and their employers an average of 1½%. Reporting this, a correspondent of the *Manchester Guardian* (April 19) quotes a statement that the cost of bringing a further 20 million citizens into a health and social-security programme will be a tax increase of about 50% on the pay-rolls of those middle-class employees now insured.

Lord MORAN has been re-elected president of the Royal College of Physicians of London for the ninth year in succession.

Dr. J. R. CURRIE, emeritus professor of public health in the University of Glasgow, died in Edinburgh on April 13.

Dr. J. W. BONE, treasurer of the General Medical Council and formerly of the British Medical Association, died on April 14 at the age of 79.

1. Gibbs, E. L., Gibbs, F. A., Fuster, B. *Arch. Neurol. Psychiat.* 1948, 60, 331.
2. Lennox, W. G., Gibbs, E. L., Gibbs, F. A. *Ibid*, 1940, 44, 1155.
3. Belinson, L. *Amer. J. ment. Deficiency*, 1947, 52, 9.

Digitized by Google

Special Articles

THE SCOPE OF THE MEDICAL ILLUSTRATOR

SYLVIA TREADGOLD
SENIOR MEDICAL ILLUSTRATOR, GUY'S HOSPITAL MEDICAL SCHOOL

FOR centuries the medical artist has been illustrating textbooks for doctors; but, when photography became widely used, it was supposed that this more scientific, accurate, and cheaper medium would render the artist obsolete. Most of the plain record side of this work is now done by photography, but the medical artist, far from becoming extinct, is now becoming a necessity in a modern teaching hospital.

The greatest difference between the pre-war medical artist and the modern medical illustrator is that the former worked on book illustration almost exclusively and for one author or publisher at a time, whereas the latter works for his hospital, not only drawing and painting but also correlating all visual teaching material.

The artist has definite advantages over the photographer. He can simplify and emphasise salient points and can create imaginary drawings of subjects not obtainable to photograph. He can suggest the feel of a thing pictorially, where a photograph of the surface would show nothing. Drawings of an operation can exclude unnecessary towels and instruments, and include anatomical landmarks not otherwise visible. A composite drawing can show what perhaps six photographs would not make clear, and humorous cartoons can catch the interest and forcibly impress a point. Though photography cannot do these things it can do others better and faster than the artist; it can, for example, serve as a basis for large accurate drawings, or provide a check on the scale and position of instruments in a complicated operation field. Some of the work done by the artist now will certainly be done by the camera in the future, when colour prints are reliable and cheap and endoscopic photography is perfected.

The production of displays and exhibitions of all kinds, graphs, wall charts, diagrams for motion pictures and filmstrips, drawings of operations, pamphlets for patients on exercises, &c., and posters for the outpatient hall are all the work of the medical illustrator, besides the traditional work of textbook illustration. Some other less known tasks are the modelling and painting of facial prostheses and the casting and moulding of models for demonstration. In America some art departments hold classes for teaching medical students to draw so that they can make their notes more easily, and for teachers on blackboard drawing. Some doctors, with only the minimum of tuition, can often make their own illustrations better than the artist can, since they know exactly what they want shown.

From these examples it will be seen that the medical illustrator must have a wide and long training. He must be primarily an artist (with the accompanying temperament well under control), able to draw and paint anything in any medium, and he must also have some knowledge of casting and modelling. He should be familiar with commercial art, lay-out, and lettering, and have an interest in modern display and be able to use it with dignity and restraint. He should know the limitations of the various methods of reproduction and their relative costs, and will find it necessary to have a knowledge of photography, especially in relation to ciné work. Above all, his medical knowledge must be at least equivalent to that of a nurse or a physiotherapist, on which his knowledge of surgery and pathology will grow with experience.

At present there is only one official school for training medical art students in Great Britain, though a few students serve an apprenticeship to established artists. The disadvantage of apprenticeship is that the student generally has little chance of seeing the work done in other hospitals, and on seeking employment may be asked to do work strange to him. The U.S.A. now has several schools of medical art giving a very thorough training. As a rule this covers a period of two or three years in the hospital after the student has graduated from an art school. The curriculum includes the dissection of a cadaver and the drawing of every stage, the practice of drawing in the operating-theatre, the theory and practice of photography, and the technique of moulage. It is hoped that some such training will soon be available more widely over here.

DRAWINGS FOR REPRODUCTION

Up to the beginning of the twentieth century illustrations for books were mostly reproduced by the engraver or the lithographer; hence much of their beauty and accuracy depended on the skill of these craftsmen. Nowadays, with the many photographic means of making blocks, the main responsibility has fallen back on the shoulders of the artist. Engraving and lithography will always have their own beauty, but they are out of place in a modern medical art department, since their cost would be unreasonably large.

A drawing or painting that is not intended for publication can be in any medium, but one that is to be reproduced must conform to the limits of the particular process to be used. Illustrations fall roughly into three main groups: line, half-tone, and colour. The first is the cheapest, and the last the most expensive.

Line drawings (fig. 1) must be done in indian ink, with proper regard to the method and size of reproduction, reduction being always an advantage, but drawings should never be enlarged. If they are to be photographed (as for a lantern slide), fine detail will tend to clog on the negative and so disappear on the positive; but, if they are to be made into a line block, fine detail will tend to clog on the final print and may appear only as a blot.

Mechanical tints may be used with a line drawing to give the appearance of a grey tone while still using a line block (fig. 2). They consist of a screen of tiny dots or lines and may be obtained in a number of shades. Kept in stock by the printer, they are ordered by number from his catalogue. The area to be shaded is indicated by colouring the drawing with a light blue chalk or wash. Particularly suitable for graphs with columns and simple diagrams, they have a more finished appearance than hand shading and, if not too elaborate, are usually cheaper.

A material gaining much favour in medical work today is scraper-board. This is a thin card coated with a layer of china clay, which gives it a smooth hard surface.

Fig. 1—Line drawing designed for a wall chart and a pamphlet, showing typical age of patient with pertussis and typical night attack.

Digitized by Google

Ideal for pen-and-ink work it may also be painted with ink, and then the surface scraped away to reveal the white beneath. It is always easier to scrape a line than to draw it with a pen; so this medium is very suitable for fine detail as well as for bold effects (fig. 3). Screened scraper-board has a mechanical tint on it giving a grey tone; so black lines may be drawn and white lines scratched on it giving a considerable range of tone all reproducible on a line block.

Half-tone drawings are generally done in carbon, lead pencil, or wash. Carbon pencils give a richer black than do lead pencils but are more easily smudged, whereas wash drawings are ideal for a half-tone block but take much time and skill to do and easily become laboured in the striving after accurate detail. Embossed scraper-board, originally developed by Max Broedel, is now widely used in the U.S.A. for medical illustrations, and is just beginning to reappear on the market here after a tentative appearance before the war. It differs from the plain variety in having a finely grained or velvet surface which will take pencil or chalk as well as ink and water-colour. Carbon pencils are most commonly used, and the drawing is worked up with a stump. Dark accents can be put in with a pen and ink, and highlights are scraped out (fig. 4). A brilliant "wet" look is obtained far more easily with embossed scraper-board than with any other medium. One disadvantage that all scraper-boards have is that of fragility, and they must always be mounted on stiff card.

The half-tone process by its nature produces a very pale tone over the white areas of a drawing. This can be removed by means of "routing" on the block, and the removal of the background tone or certain highlights may make an illustration stand out boldly (e.g., the familiar 'Persil' advertisements), but it sometimes has the effect of making it "jump" from the page. For this reason, if white lettering, arrows, &c., are to be added to photographs they should always be put on before the print goes to the blockmaker. If they are routed on the block they will become too predominant, besides which, the fact that such work is done by hand will considerably increase the cost of the block.

Colour reproduction, other than line work, does not always give correct colour rendering, and the cost is extremely high. The artist is advised to make close contact with the printers so that he can conform as closely as possible to their limitations. Paintings meant for permanent records, whether for reproduction or not, must be done in permanent colours. These can be obtained in water-colours, oils, and draughtsman's colours, but poster paints, coloured inks, and crayons are never guaranteed in this respect, and the colours are sometimes extremely fugitive.

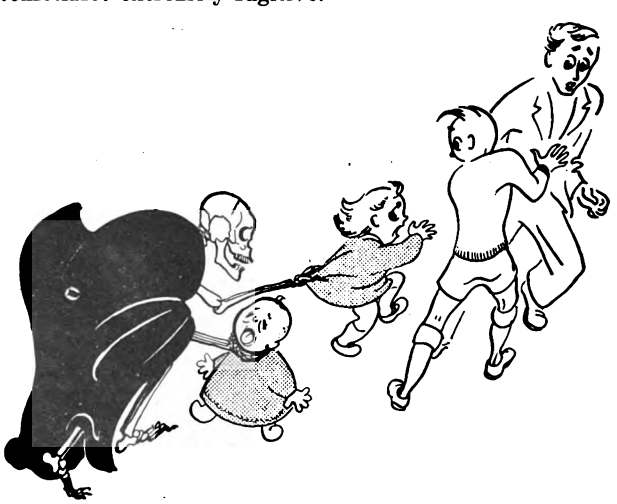


Fig. 2—Cartoon in line from a series of teaching charts on pertussis, showing ages most likely to succumb. (Note mechanical tint, or stipple, on clothing of two smallest children.)

MOTION PICTURES

This visual medium now has a much higher standard than it had before the war. Then a film was more of a curiosity than a teaching medium, made more for the fun of creation than for its potential use. Now students are far more sophisticated and expect first-class photography, accurate rendering of colours, diagrams (animated or otherwise), and good editing. A film giving less than this will merely attract attention by its faults.

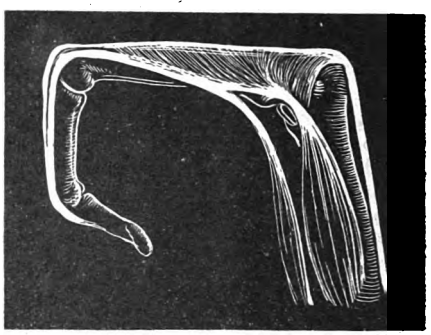


Fig. 3—Drawing on plain scraper-board, showing the digital "extensor hood" with muscle attachments.

The medical illustrator should be present with the photographer at the initial discussions for a film, so that technical limitations can be realised at the start and each knows the part he has to play.

Diagrams should be bold in treatment, and when intended for use in a colour film they should be in the brightest colours, or they will appear very pallid, especially in an operation sequence. White backgrounds must be avoided since they tend to glare; in general a mid-toned neutral colour is most satisfactory (fig. 5). Too realistic drawings should be avoided, since they cannot but lose by contrast with the photography, and this applies also to the colouring of them.

Labelling is best done on separate sheets of celluloid and laid in accurate register over the diagram, so that each word or phrase can appear separately. This is much more readable than having all the labels appearing at the same time. The lettering should not be less than $^1/_{32}$ of the height of the frame, and in a simple clear type, capitals if possible, and sans serif.

If much *animation* is to be used, other than the simple sorts which can be done by the photographer, the work should be farmed out. This will prove more economical (though still costly) since it is a slow, tedious, and difficult job to someone not trained to it. The key drawings are sent to a studio specialising in this type of work, and they produce the linking pictures.

FILMSTRIPS

As with a film, the artist doing filmstrips should be in possession of the script so that drawings can be related to each other in treatment and tone. White backgrounds should definitely be avoided, a mid-grey tone proving most satisfactory. Though the loss of detail on projection is not so great as in a film, drawings should still be done in a simple and bold manner—the key prints of photographs being used often need retouching because of this. Though not essential, it is often more convenient to do captions and labels on celluloid and to superimpose over the print or drawing. The smallest lettering should be not less than $^1/_{40}$ of the height of the frame.

Though strips can be made from various existing illustrations, it is advisable to have them redrawn in most cases, since they are often lacking in contrast or have too fine lines or too small labels. A strip to be good should have as much thought and production put into it as a film, and it is not therefore a waste to have drawings done specially for it.

LANTERN SLIDES

Though so often used, slides are still commonly illegible for one reason or another. Too much on them,

Digitized by Google

too small lettering, and too thin lines are perhaps the commonest causes. The medical illustrator can help by advising on the size and amount that are suitable on a slide. If it is a graph, line drawing, or lettering, it will be more legible if the finished slide has white lines on black than vice versa. Lower-case letters and italics should be avoided unless amply big, and where possible the letters should be well spread out. If the smallest lettering legible under the worst projection conditions in the hospital is determined from the back of the lecture hall this can then be kept to as a standard—e.g., our smallest lettering for $3^1/_4$ in. slides is $^1/_{40}$ of the frame height, if the finished slide has white letters on a black backgroumd.

WALL CHARTS

The first necessity for wall charts is legibility at the distance from which they are to be seen. They may range from a 6-ft. chart to be seen from the back of the lecture hall to the small series as big as postcards running round a room for reference or study in a spare moment (fig. 6). They often successfully incorporate photographs and must be attractively drawn and coloured, so that passers-by will stop to study them. A poster technique can be used when they are to appeal to the patient or to relations in the outpatient hall, but in the classroom one should never be conscious of the skill of the artist, but only the

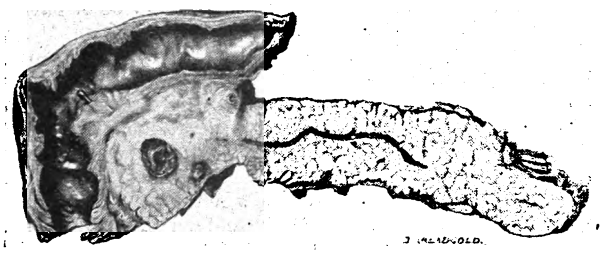


Fig. 4—Drawing on embossed scraper-board (here reduced by two-thirds). Specimen showing carcinoma of head of pancreas.

clarity of the information presented. Stiffened and covered with cellulose acetate (about 0·003 in. has been found very satisfactory) they will stand up to a long life of wear and tear.

EXHIBITIONS

With exhibitions the medical illustrator must have sufficient time and know at first the amount of material and information to be presented. Nothing looks worse than last-minute notes stuck in at odd places in an otherwise well-designed and coherent display.

A monthly exhibition of, for instance, some surgical or pathological subject has already proved of great help

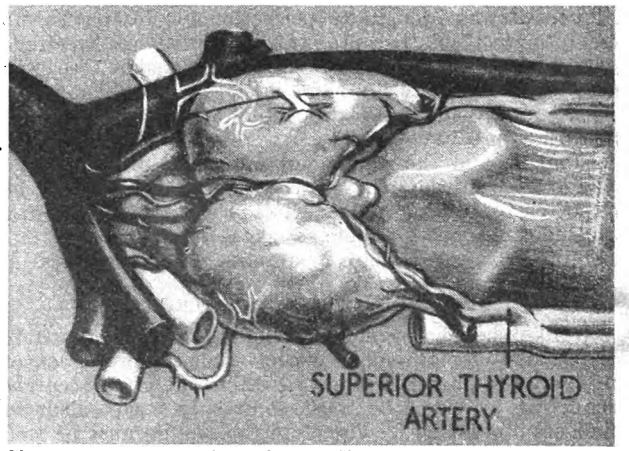


Fig. 5—Diagram (in colour) from a film on thyroidectomy, showing comparatively coarse technique and large lettering.

to medical students and nurses, and it is of general interest to nearly everyone in the hospital.

Doctors on the whole are very easy to please with exhibition work, for they apparently do not notice the high standards of public exhibitions. Though this may be easier for the illustrator now, he must be abreast with modern display methods, and undoubtedly his public will become more critical as more of this work is done. Photographs, paintings, specimens, models, diagrams, instruments, books, cartoons, &c., may all be used to demonstrate the anatomy, pathology, clinical features, treatment, &c., of the subject.

If regular exhibitions are to be held, it is best to have stands built to hold pathological specimens, &c., at eye level and with a suitable background. A specimen on a table is always difficult to see—it needs to be picked up, and is then often put down in the wrong place. Teaching-charts too need to be supported at an angle where the light does not reflect on them and they are easily legible.

Colour is most important in an exhibition, and, though it should be kept traditional in anatomical diagrams, there need be no limit to the variety elsewhere. If, for instance, all material to do with treatment has green introduced somewhere, this will make it easily distinguished even though it is not all placed together. Coloured strings, tapes, mounts, and even matting on the floor are useful for producing these colour links.

MOULAGE

This is the technique of casting or moulding in wax, and is so far more used in America than over here,

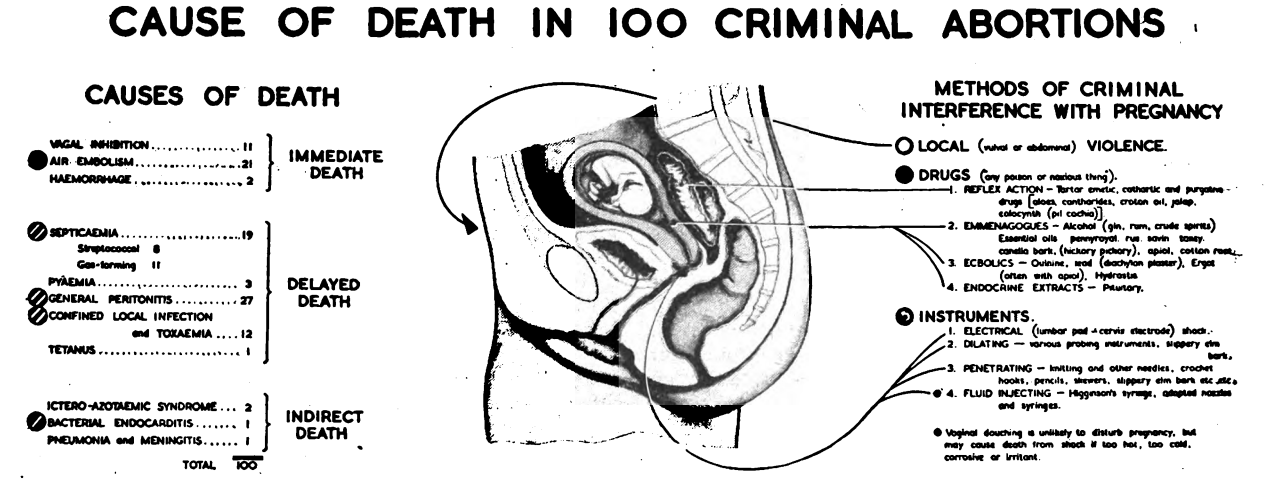

CAUSE OF DEATH IN 100 CRIMINAL ABORTIONS
CAUSES OF DEATH
VAGAL INHIBITION 11
AIR EMBOLISM 21
HAEMORRHAGE 2
IMMEDIATE DEATH
SEPTICAEMIA 19
Streptococcal 8
Gas-forming 11
PYAEMIA 3
GENERAL PERITONITIS 27
CONFINED LOCAL INFECTION and TOXAEMIA 12
TETANUS 1
DELAYED DEATH
ICTERO-AZOTAEMIC SYNDROME ... 2
BACTERIAL ENDOCARDITIS 1
PNEUMONIA and MENINGITIS 1
INDIRECT DEATH
TOTAL 100
METHODS OF CRIMINAL INTERFERENCE WITH PREGNANCY
LOCAL (vulval or abdominal) VIOLENCE.
DRUGS (any poison or noxious thing).
1. REFLEX ACTION – Tartar emetic, cathartic and purgative drugs [aloes, cantharides, croton oil, jalap, colocynth (pil cochia)]
2. EMMENAGOGUES – Alcohol (gin, rum, crude spirits) Essential oils pennyroyal, rue, savin, tansy, canella bark, (hickory pichory), apiol, cotton root,
3. ECBOLICS – Quinine, ergot (cockyhon plaster), Ergot (often with apiol), Hydrastis.
4. ENDOCRINE EXTRACTS – Pituitary.
INSTRUMENTS.
1. ELECTRICAL (lumbar pad + cervix electrode) shock.
2. DILATING – various probing instruments, slippery elm bark,
3. PENETRATING – knitting and other needles, crochet hooks, pencils, skewers, slippery elm bark etc. etc.
4. FLUID INJECTING – Higginson's syringe, adapted nozzles and syringes.
Vaginal douching is unlikely to disturb pregnancy, but may cause death from shock if too hot, too cold, corrosive or irritant.

Fig. 6—Display panel 20 × 60 in. The circles by the headings are colour links both to the central printing and to other exhibits in the exhibition. (Reproduced in line and half-tone.)

Digitized by Google

chiefly through lack of personnel trained in the technique. It was brought to perfection by Joseph Towne (sculptor to Guy's Hospital 1826–79) with his hundreds of models of anatomical dissections and skin diseases; his secrets died with him, and such a standard has never been equalled since. Plaster, latex, and various plastics are other mediums useful for making models.

Moulage and the making of models take much time and study on the part of the artist, who cannot be expected to do it as well as a full programme of drawing and painting, but for some subjects—e.g., where the feel is important—models are unsurpassable for teaching.

ACCOMMODATION AND MATERIALS

Unlike the photographer, the artist depends entirely on daylight for all colour work, because there is as yet no lamp obtainable in Great Britain that gives accurate rendering of reds (the most commonly used colour in medical illustration). Therefore the studio must be well lighted, with a north light, and if possible each artist should have a window to himself. With a poorly lighted room all colour work may be entirely stopped during some of the winter months. Working from the patient in the studio is greatly preferable to a busy ward or out-patient department; therefore suitable accommodation for this is important.

Thought should be given to whether the artist is to store the finished work (the better method) or whether it is to go to the various departments that have ordered it. In any case some standardisation of sizes will facilitate storage. If, for instance, large charts are kept to Imperial size (30×22 in.), two piles may be stored in an antiquarian-sized plan-chest (54×33 in.), and smaller charts, if limited to 15×12 in., may be stored on edge in the ordinary steel filing-cabinet, where they are easy to get at, and have the minimum of rubbing.

Each artist will require at least one drawing-table; (30×40 in. has been found a very useful size), and a parallel-motion T-square is particularly useful when much stencil lettering is done. One plan-chest will be needed for stocks of paper, the choice of which, together with the paints, &c., should be left to the artist. Lettering stencils are now obtainable in several different alphabets; and, though considered by some as unæsthetic, these are great time-savers and invaluable where several artists are working on, say, an exhibition, because the lettering is then unified. They are designed for legibility and so are particularly good for labelling lantern slides and diagrams for reproduction.

Owing to the lack of knowledge about the work of the medical illustrator there are still stupid misuses which waste time, skill, and money on both sides. A drawing is asked for when a photograph would be better, or diagrams are requested of no specified size or technique, and are later found almost unrecognisable through bad reproduction and clumsy labelling by the printer. Insufficient time is given for work which needs thought and originality; hence the work becomes scamped and may be still further spoilt with last-minute corrections of data which should have been done before the request ever reached the studio. Often the artist is told "a rough sketch will do," and will not be given the time to do anything more—yet the result is grumbled at for its insufficiency.

Much of this ignorance is due to the very little interchange of teaching material between hospitals. So much of this work done particularly on pamphlets, filmstrips, and motion pictures could have a much wider circulation than it now gets, and it is hoped that some such exchange will take place more often in the future.

CONCLUSION

The medical artist and the photographer are both essential to produce all the various visual aids applicable in a teaching hospital. Each has advantages over the other in his own field of work. It is hoped that wider knowledge of the use of the medical illustrator will lead to a higher standard of teaching material, and that in the future this will be exchanged more widely between hospitals and clinics.

I wish to thank members of the medical staff of Guy's Hospital for permission to publish the illustrations, which have been done by the department of medical illustration of Guy's Hospital medical school.

THE HEBREW UNIVERSITY HADASSAH MEDICAL SCHOOL

ELI DAVIS
M.D., M.Sc. Manc., M.R.C.P.
DIRECTOR, HADASSAH MEDICAL ORGANISATION

THE Hadassah Medical Organisation has made important contributions to medicine in Israel. In the days of the mandatory government its task was to set high standards, to attract and train skilled staff, and to build up specialised departments otherwise lacking in the country. Under the dynamic leadership of Dr. H. Yassky the organisation attracted able physicians from Europe and the Anglo-Saxon countries and established a model nurses' training-school in Jerusalem. The outstanding event in all these efforts in the service of patient and profession in Palestine was the opening on Mount Scopus in 1939 of the modern, well-staffed, well-equipped Hadassah-Rothschild University Hospital and the Ratnoff laboratories for clinical investigation and research. In this medical centre a tradition of sound postgraduate training was established.

In addition to its curative services, Hadassah established throughout Palestine a network of preventive medical services which set the standard in child welfare and maternal care. During recent years Hadassah has consistently directed its efforts in such a way that its hospital and medical services would form the basis of the clinical part of the future undergraduate medical school to be established in conjunction with the Hebrew University in Jerusalem.

During the battle for Jerusalem in 1948, Hadassah took on responsibilities similar to those of the Emergency Medical Service in England during the war; its surgical teams effectively treated most of the casualties in the Jerusalem zone. When the medical centre on Mount Scopus was cut off after the ambush and massacre of medical and university staff on April 13, Hadassah set up in Jerusalem town a series of emergency hospitals which saved the medical situation in Jerusalem and which was a vital factor in maintaining morale.

It might have been thought that in these circumstances the whole medical-school idea would have come to a standstill. But Hadassah continued to act as the pace-maker in this project. For many years there has existed in Jerusalem a pre-faculty of medicine, planning steadily and patiently for the Palestine medical school of the future and helped always by the New York medical reference board of Hadassah and the Hebrew University. Indeed, in the year preceding Israel's war struggle, new buildings to serve the basic medical sciences had begun to be built on Mount Scopus. In addition, Hadassah's widespread preventive medical service had been built up in such a way that special facilities could be offered to medical students to enable them to become preventive-medicine minded and real public-health servants. Despite the death of the leading personalities in medical-school planning in the ambushed convoy (Dr. H. Yassky, Dr. L. Doljansky, and Dr. M. Ben David), the very circumstances of war gave a tremendous spurt to the idea. Moved by the devotion and the zeal for the medical school so manifest in Jerusalem and Israel, Hadassah

Digitized by Google

in America undertook to provide much of the building fund and a good deal of the maintenance budget for the Hebrew University Hadassah medical school. Meanwhile Israeli medical students were recalled from abroad to serve in the defence army. When the possibility of freeing them from paramilitary duties arose, the army command discussed with the authorities of Hadassah and the Hebrew University the question of those students completing their training. Dr. A. Dostrovsky, dean of the medical faculty, together with his colleagues of Hadassah and the Hebrew University, accepted the responsible task of opening up a medical school with these soldier-students forming most of the first class.

At the time the task was accepted we had no adequate buildings in Jerusalem town, Scopus still being cut off. On the other hand, we had the teachers necessary to turn a curriculum into a reality. Suitable buildings were found and the work of adaptation and of repairing war damage begun with vigour.

We are enrolling 45 students this April, selected from among 200 applicants. All of them will have satisfied the faculty as to their character and good educational background. This particular group of students will have had recognised training abroad—and passed appropriate tests—in anatomy and physiology, and will be given the following course: One year in basic medical sciences (preclinical), two years of clinical training during which time preclinical disciplines will continue to be taught, and one year of practical study in hospitals recognised by the faculty. Throughout the period of training, emphasis is to be put on preventive and social medicine. We are fortunate in having a nucleus of experienced teachers and an ever-growing group of able young physicians and scientists who have returned to Jerusalem after having had the benefit of special training and experience in some of the great medical centres abroad and particularly in the U.S.A.

The stage is now set for the official opening of the first undergraduate medical school in Israel, in Jerusalem on May 17. This date is the traditional scholar's day in the Jewish calendar—the 33rd day of the Omer, the day on which a plague which threatened to kill all the disciples of the famed Rabbi Akkiba was stayed.

We will do our best to develop a school worthy of medicine, our students, and our sponsors.

BRITISH MEDICAL STUDENTS' ASSOCIATION

CLINICAL CONFERENCE

THE third national clinical conference organised by the British Medical Students' Association was held in Cardiff from March 28 to April 1. It was attended by 66 delegates from fifteen different medical schools, including Trinity College, Dublin.

In his presidential address Prof. Ralph Picken, provost of the Welsh National School of Medicine, observed that "if you see and hear things here which differ from what you have learned in your own schools, we shall feel that we have dealt faithfully with you."

The clinical programme centred around the Cardiff Royal Infirmary. The teaching staff coöperated with the student organisers in arranging an attractive programme of ward-rounds, lectures, and demonstrations both in general medicine and surgery and in various ancillary subjects. Groups of delegates also visited certain more specialised hospitals. The programme was designed to show some of the medical problems peculiar to South Wales and some of the work which has been done locally. Thus it included a lecture-demonstration on pollen allergy by Mr. H. A. Hyde and Dr. D. A. Williams; an account by Dr. Derek Richter of the biochemical research which has been proceeding in his unit at the City Mental Hospital; a lecture by Mr. Dillwyn Thomas on a new approach to the surgical treatment of pulmonary tuberculosis; a lecture on corneal grafting by Mr. J. W. Tudor Thomas; a demonstration of the technique developed by Prof. J. Gough and Mr. J. E. Wentworth for cutting and mounting whole sections of tissue on semi-transparent paper; and a visit to the premature-baby unit and milk bank at St. David's Hospital, under the direction of Dr. Jacobs.

One whole day was devoted to the subject of pneumoconiosis. In the morning, Dr. C. M. Fletcher, director of the M.R.C. pneumoconiosis research unit, met the delegates at Llandough Hospital and spoke on the general and clinical aspects of the disease. Later, a lecture by Dr. Warner, of the National Coal Board, introduced the delegates to some of the mining problems associated with the suppression of dust at the coal face. In the afternoon groups of delegates visited three collieries and examined dust-suppression measures in the pit.

On the night of their arrival the delegates were entertained at an informal party given by the Cardiff Medical Students' Club. Other social activities during the week were a civic luncheon given by the lord mayor of Cardiff, a dinner given by the medical board of the United Cardiff Hospitals, and a dinner and dance on the last night.

The social arrangements have some importance because the popularity of such conferences as this seems to indicate that medical students seek the refreshment and stimulus provided by contact with other students and teachers. The association hopes that clinical conferences will be held twice a year in different teaching centres, and that the organisers will pay as much attention to social activities as to the formal clinical programme. The Cardiff conference benefited by sympathetic encouragement from the authorities of the medical school and from the board of governors of the United Cardiff Hospitals; and the board's grant of up to £200 towards expenses enabled the cost per delegate to be kept to a figure which allowed all students wishing to attend to do so.

Disabilities

28. FRACTURED SPINE

MY Labrador began it, and being a much-loved dog he gained his wish, and a strenuous tug-of-war took place in drizzling rain one summer morning before breakfast. In the heat of the contest we rushed to the top of a bank, and then something gave way. A human body shot, as though from a catapult, out from the bank for a considerable distance, and then crashed, in a sitting position, on to the tennis-court below.

When I came to my senses I realised that death was very near. I knew, quite definitely, that if anyone came and tried to move me, or even if I moved myself, all would be over; so I remained a motionless heap, just conscious of the presence of my dog, who walked round and round me, sniffing as he went. How long I crouched there I do not know, but with returning consciousness came the pain, which seemed to envelop me—such terrific pain that for months afterwards I shuddered if I thought of it. Again and again I felt that the intensity of it would kill me, and I groaned in anguish. Slowly I began to realise that somehow I must get back to the house, and when I began to move I found, for the first time, that I was quite blind: I could see nothing but black emptiness. But I knew the direction in which the house lay, and slowly crawled across the lawn, down a grassy slope, across the drive, and up a few steps into the house, and collapsed into a big chair in the hall.

I heard someone coming downstairs and managed to gasp out the word "fall," for I thought that the end

Digitized by Google

had come and no-one would know what had caused my death. My family thought I was dead, and I was pulseless when medical aid arrived. I remember being carried upstairs and laid on my bed, and by this time my sight had returned. When the first shock had passed I was able, with help, to stand up while I was undressed, this being quicker and less painful than being moved about in bed.

Fortunately the spinal muscles had gone into intense spasm, making my spine absolutely rigid. Thanks to this natural splint the pain, on the whole, was bearable, though at times there were almost unendurable paroxysms. The ordinary sedatives were quite ineffective, and I refused morphine compounds because I wished to keep my brain as clear as possible. It was necessary for me to make as light of my accident as I could; and in this I was aided by my secretary, who nursed me devotedly throughout. I could be bright and chatty for about 10 minutes at a time, and then my visitor was dismissed and I was left alone to wrestle with the pain. I always found I could endure it better if there was no-one near me.

After two days I decided to have a bath. My back was still rigid, so I was able to shuffle slowly into the adjoining bathroom and be lowered on to a rubber mat in the bath. I steadied myself, when seated, by holding on to the sides. The hot water was very soothing and the comfort of it was worth the effort it entailed, so I had a bath daily.

Five days after the accident I got up, was partially dressed, and was then driven a distance of nine miles to undergo an X-ray examination. The following day I went the same distance to consult my dentist about a tooth which was being very troublesome. The ability to manage these two excursions was due to the persistent spinal rigidity and to the fact that the car was driven very slowly and very carefully. The radiological report came just as I had returned from the dentist. "A compressed fracture of the anterior and upper portion of the body of the twelfth dorsal vertebra."

A consultation was held and it was agreed, in view of my age—I was 57—not to put me into plaster. This decision was a great relief, for I felt I had reached the limit of my endurance and knew I could not have stood all the discomforts that "putting into plaster" would have entailed. Little pillows were placed in the small of my back so that the spine was hyperextended and I was in a position of opisthotonos. For several hours after I had been "arranged" I was fairly comfortable, but during the night, as the spasm of the muscles gradually relaxed, the agonising pain came on again, and early in the morning help had to be summoned. The removal of one pillow was followed by relief, and I lay like this for the next four weeks. I had been through such a severe shock that I had no wish to move and was quite content to be there motionless hour after hour. I did not realise how helpless I was until I was visited one day by a friendly little boy who came up to my bed and stretching his closed hand over me said solemnly "I have brought you a handful of little frogs from the pond."

Soon I was able to feed myself. The plate was put on my chest, I was told the position of the various things, and I managed more or less tidily. By using a hand-mirror I could watch the children if they played in a certain part of the garden. Once, when there was a garden-party, my bed was raised on very high blocks so that I could see out of the window, but the excitement and exertion soon proved too much, and I had to be lowered again. The gift of a beautiful wireless-set, with a switch on a long flex reaching my hand, greatly helped to shorten the hours. Reading, unfortunately, was out of the question; I was still too shaken to be able to concentrate. Later in my convalescence the only books which could grip my attention were thrillers, and for some time I read nothing else. At the end of four weeks I was well enough to be measured for my spinal support. For two days my head and shoulders were raised for a short time to prepare me for the great event. When the day came I was clothed in a bathing-dress, helped out of bed, and seated on a stool while measurements were taken. I don't know how long I sat there, but it seemed an eternity, and when I finally quavered out that I couldn't sit any longer, I was nearer an hysterical outburst than I have ever been before or since. Two weeks more of opisthotonos, and then the support arrived. It had a back bar, side steel bars and axillary crutches, and a stay portion in front. It was tried on and pronounced to be a perfect fit. The following day I was buckled into it and sat in a chair for a short time, a helpless lump of misery. My head, unaccustomed to the upright position, was swimming, my body was gripped in a vice and my legs seemed powerless. The second day I felt worse and nearly fainted, but as I went on getting up each day my brain became clearer and my legs gained strength. The support was made fairly comfortable by little pieces of sponge-rubber inserted at all points of pressure. As time went on I was able to discard these pads, and my body seemed to fit itself to the support until I, too, was able to pronounce it "a perfect fit."

When I tried to get out of a chair, I found I had lost all "spring" and had the greatest difficulty in getting up. Though I always sat in a high chair with a long straight back and grasped the arms to help myself, I used to fall back six or seven times before I could eventually stand upright. It was many weeks before I was successful at the first attempt. Then my balance was upset by my rigidity, and I had to learn to walk again. The control of my hands and arms was weak and I dropped everything on the floor, and of course was unable to pick it up again. Later I was able to buy a pair of extending tongs, called "lazy-tongs," and in time became adept in picking things up from the floor and reaching things I wanted. After I was able to manage the stairs I lived more or less in the garden, for it was lovely summer weather. I had looked forward to resting in a swing seat that had been given to me, but try as I would I was too "stiff and proud" to get into it. The children were home for the holidays, and greatly enlivened my convalescence. They wrote and acted several little plays for me, and four flat, tuneless voices constantly reminded me that "It's a poor heart that never rejoices." How I blessed those children as they shared with me their happiness and joie-de-vivre.

For some time I had been thinking about work, and when the colleagues who had kindly looked after me were well away on holiday I determined to make a start. I had one appointment made for me, in spite of all the sensible counsels against it. It took half-an-hour to drive to my consulting-room, and we had only gone part of the way when I felt so ill that I almost decided to turn back; but I was determined to "save face" if possible, and so managed to reach my destination and see my patient. I was so completely played out afterwards that once I was back in bed, I realised that I had attempted the impossible. It took me several days to recover, and I felt I had lost far more face than I had saved. I remained resting at home for another month, and then started work again; first one patient a day, then two, and so on; but for many weeks, when I reached home, I lay prostrate on my bed for two to three hours, hardly conscious of anything around me. Then I revived in an amazing way, got up, had dinner in my room, and attended to my correspondence.

Digitized by Google

At first I was driven in a coupé car, for I could not get into the saloon. It was quite easy to get into the front seat when the car was open, but if it rained the hood had to be lifted and let down again each time I got in or out. This wasted time, so I tried the saloon again and eventually evolved a technique which proved highly satisfactory. I was more or less handed into the car, like a large parcel, at an angle of 45°, and deposited on the seat, my legs being lifted in afterwards. This was tiresome at first, but in a short time I was able to swing myself in quite comfortably and quickly; it served its purpose, though it was hardly a dignified performance for an elderly practitioner. Since I was unable to bend, the examination of patients offered a problem at first, but by kneeling down by the couch or bed I managed well, and my patients soon became accustomed to seeing me flop down on my knees. I always explained my difficulty to new patients, for I thought they might be somewhat alarmed to see me suddenly go down on the floor. In hospital my method of examination was treated with the greatest respect. When I did my rounds a probationer nurse came at the end of the procession carrying a nice firm cushion (on which my initials were embroidered!) and this was always solemnly placed in position before I knelt down.

As time went on I became more confident in my walking and less clumsy. So one day, when near home, I dismissed the car saying I wished to do some shopping and would walk home. On crossing a small side road I somehow fell flat; my parcels flew in all directions and I lay there helpless. The kindly folk who came to my assistance were naturally surprised at my rigidity; they had to pick me up bodily and stand me up like a tin soldier. I returned home greatly shaken in mind and body.

After a year a second X-ray photograph was taken, and as it was entirely satisfactory my jacket was discarded and I had a spinal brace with an abdominal corset and axilla straps. It took me some time to get used to it, and I often felt tempted to go back to my trusty friend, the "strait jacket," in which I felt secure and safe. At the end of two years, however, I was able to discard all supports, and so was able to drive my car once more. I was also able to do a full day's work, though my former energy had not completely returned.

A tiresome sequel to the accident was insomnia. I had always been an excellent sleeper, but for over a year I had to take a strong sedative each night. Again and again I tried to dispense with it, but the only result was a night of complete wakefulness, followed by a day of wretchedness and pain. At last, after a holiday in the country, my habit of sleep was restored, and it has never been broken since. The only disability that remains is stiffness of the lower spine, which makes me unable to turn; if I attempt to do so I am seized with a sharp sickening pain which lasts for some time. I have therefore learned to avoid any such movement. Backing my car into a small space is impossible unless I have someone to guide me. In the various parking-places an attendant is usually present; but if not, and if there is no-one else about to whom I can appeal, I have to find another resting-place for my car. This, however, does not often happen.

Overwork or overstrain always brings back a modicum of pain, but this can be abolished by lying down with the spine hyperextended. I cannot sit comfortably in a lounge chair, so always choose one with a high straight back. My activities have not been curtailed in any way, and I have been able to take my full share of medical and social work, without being hampered by any major sequelæ to the accident which so nearly proved fatal.

In England Now

A Running Commentary by Peripatetic Correspondents

WAS there ever such an Easter? Sunshine and cherry blossom; sunshine and butterflies; sunshine and bathing. Never quite thirteen to meals, and hardly a cross word for four days. Nobody tipped out of the gig, and eight eggs in the moorhen's nest on the island. Perhaps everything else In England Now will go well henceforward.

Colin brought in two derelict baby grey squirrels. With closed eyes and long smooth tails, they looked even worse than baby rabbits, and equally moribund; but one is still alive on milk and water from a rubber ear syringe. Mrs. Parks said the milk must be mulled with a red-hot poker, and no doubt that's the secret. Test feeding on the kitchen scales (with an experimental error of 100%) showed that something like half its own weight can be got into a squirrel at each of its irregular meals. No night feeds, but a hot bottle instead.

Talking of Nature, I feel sure we could learn more by examining the close parallels between animal and human behaviour. For example, some observations I made while doing the autumn digging on Easter Day seem to bear closely on feminism, family allowances, and so on. The cock and hen robin, you will remember, are indistinguishable in plumage—but how extraordinarily different is their conduct! With rumpled feathers and haggard eye, the breadwinning cock was continually in and out of my trench, darting daringly under the spade to grab half a dozen centipedes and little worms, which he carried untasted to his brood. Yet for some time the hen did not so much as appear at all; and when at least she came—svelte, soignèe, negligent, and remote—I was shocked to see that her rare and casual catches were all eaten on the spot, without a thought for those at home.

Easter, I felt, was possibly not the moment at which to mention these observations to my wife. We biologists must be prepared for a certain intellectual loneliness.

* * *

The past twelve months have been better altogether: first the Budget surplus and now the annual harvest of the Royal Society of Painters in Water Colours. Quite a number of the pictures, this year, are different. More are the same, of course. I believe that in all picture shows there is a permanent substrate which is kept in the janitor's office, dusted and put up again yearly. Probably there is some technical reason for the practice—it maintains continuity, helps the eye to modulate, favours hypnosis, or simply reminds one this is a picture show. I don't know; anyhow it saves a lot of time.

Whenever I go into that pleasant rectangular gallery in Conduit Street I become a Coke addict. I don't mean what is called (but I may be out of date), in criminal circles, a snowbird; but an enthusiast for Miss Dorothy Coke. Her pictures, often signed by the cat, are as shrewd and witty as a page from *Persuasion*. This time the cat appears on the sill of the "China Shop, Brighton," and I am sorry to note that he seems to be getting on; his ginger coat grows dim and dusty—or else he was subduing himself, chameleon-like, to the subtle colour values. The little picture is an epigram, from the bellying classical figure above to the peering backs below. Mr. A. Sillince has some witty ones, too: "Shoppers," and "Sunday" at the Chelsea Hospital, where the coats of the pensioners nicely suit his cartoonist's style. The year has been wet, windy, and full of Scotch mist, some of it so thick you can hardly see the picture. I was glad to be in out of most of it, but I wouldn't have minded seeing (through a window) that moment in the "Essex Marshes" which took W. A. Wildman's notice. A monstrous cloud was letting down a hedgehog fringe of rain on water filled with primrose light and greenish-blue reflection. Dame Laura Knight's "Quick Change," where the actress in a dim delphinium petticoat stands waiting for the next dress, is more agreeably coloured than her "Theatre Productions" or "Ringdoves." Robert Austin had also gone

Digitized by Google

behind the scenes to find a "Ballet Student Resting," with shoulders sagging and solid legs crossed—a faintly pink drawing which takes the eye.

Bird painters can always count on attention nowadays, and Mrs. Grace Wheatley gives unusual pleasure with her delicate bluebirds and diamond doves. But one does not need to be a bird-watcher to turn the head for Mr. Keith Henderson's crested barbets and sunbirds. Barbets are violently clad in orange, yellow, white, black, blue, and grey; and Mr. Henderson says so, and says it loud and clear. His sunbirds, among butterflies and pink-flowering aloes, are purple, green, and red. The dazzled eye, bred to the English climate, turns gratefully to another Wildman—"Regatta Week, Burnham-on-Crouch," a wettish festival by the look of it, well adapted to the national taste.

* * *

Returning to my hotel one night in New York I saw that a lecture on "Craniopathy" was advertised to begin almost immediately in a building nearby. I went inside to learn what I could. The audience was small—only about 14, mostly osteopaths. The lecturer was a lady who said she was over 70 and had travelled all over the world teaching her particular doctrine. The gist of her lecture was as follows. The skull is composed of many bones closely articulated together, but fortunately the bones of the vault are separated by a mucous membrane which allows considerable movement between them, and thus by manipulating the skull it is possible to relieve pressure or tension on the nerves which issue from it. By this means many nervous disorders and even general diseases can be influenced—for example, the lecturer claimed that skilful manipulation of the skull would cure hip disease and diabetes. She offered to teach us her methods in a course of lectures, for a consideration which she assured us was a considerable reduction from her usual fees, and she offered us our money back if we were not satisfied with our results. It should be added that this lecture was free, but no secrets of technique were given away.

* * *

To learn on Budget day that my telephone is going to cost more was a shock. It's bad enough paying extra for meat and margarine, but to pay more for something one dislikes is the unkindest cut of all.

As a child I was scared of the phone, fearful of not being able to hear what was said, fearful of not being able to take down a message correctly. I looked on it as an infernal invention—something to be treated with the greatest respect. People to whom in ordinary life I would talk quite casually, acquired a new dignity on the phone. Everyone must stop talking while they spoke, and above all they must not be kept waiting. In those days a telephone call was an event. It's different now. The phone bores and annoys but seldom pleases. Why does it always ring when I'm most busy? When I'm attempting to listen to a patient's tale of woe, write a prescription, and take a call the instrument is treated with scant respect. If the caller does not answer at once I prop it up on the desk, hoping that in time the operator's voice will become loud enough to be heard through my patient's discourse, or, even more difficult, through the chest-piece of my stethoscope while it is applied to the small area of chest allowed by the utility vest. However, if I don't hear, my patient most certainly will.

A telephone bell is bad enough during the day, but at night it is ten times worse. At night my childhood fear of the phone comes back. I dare not wait a moment before answering it. I am afraid the caller will ring off before I have spoken. Are all people as stupid on the phone at night as I am? A name I know well will convey nothing to me, and patients' relations appear sadly hurt when I appear to know nothing of the case. But when all is said, away from home and without the phone I miss it. I hate it with a deadly hatred. Its voice never fails to infuriate me. But let it remain silent for a single morning and I ring up the exchange to accuse them of not transmitting calls. I insist it is out of order. I demand that it shall be put right at once. And when the tormentor is restored I contentedly start abusing it again.

Letters to the Editor

LIVER EXTRACTS

SIR,—In recent correspondence microbiological assay has been mentioned as the most promising method of standardising liver extracts. This method has demonstrated that material apparently identical with vitamin B_{12}, the liver anti-anæmic factor, can be obtained from other natural sources. It has been shown that certain micro-organisms can produce vitamin B_{12}, and material obtained from certain strains of streptomyces has been stated to be active in pernicious anæmia.[1]

Lately I have had the opportunity of testing material, supplied by Glaxo Laboratories, produced from a similar source. This material was standardised in its vitamin-B_{12} activity by microbiological assay. The responses of patients with pernicious anæmia to doses of this material, containing 10–20 μg. of vitamin B_{12}, appear to be identical with those produced by liver extracts of comparable potency, as determined by microbiological assay. Up till now, 4 patients have been treated, including 1 with severe neurological complications; this patient has made good subjective and objective improvement as a result of receiving for the last six weeks doses of 20–40 μg. of this material weekly. It is hoped to publish more detailed results of these cases at a later date.

The development of the microbiological method of assaying vitamin-B_{12} activity in liver extracts, or in the products containing the factor derived from sources other than liver, is a great advance. It offers the prospect of accurately standardised material and, therefore, a more satisfactory basis for dosage.

Department of Pathology, Postgraduate Medical School of London. D. L. MOLLIN.

SIR,—Your reply to Dr. Murphy (April 2) makes two implications which I believe to be untrue: firstly that refined liver extracts, particularly of the Dakin and West type, are less effective than crude liver extracts in the treatment of the neurological manifestations of pernicious anæmia; and secondly, that subacute combined degeneration without anæmia is notoriously resistant to treatment.

The application of a quantitative method of assessing neurological status to the study of 44 cases of subacute combined degeneration, to be published shortly in *Brain*, revealed no significant difference between the effects of crude and "refined" liver extracts of the Dakin and West type. Moreover, in a further series of cases it was demonstrated that vitamin B_{12} itself was as effective as liver extract—crude or refined—in the treatment of subacute combined degeneration. Since part of the damage to the nervous system is irreversible these therapeutic agents "have at best only a partial effect." The chief factor influencing the response to treatment was the duration of difficulty in walking. The degree of anæmia present initially was of minor importance.

Royal Victoria Infirmary, Newcastle-on-Tyne. C. C. UNGLEY.

WERTHEIM'S OPERATION

SIR,—The generation of gynæcological surgeons trained and inspired by Mr. Victor Bonney will rejoice at his masterly presentation, printed last week, of an unsurpassed experience of radical surgery in the treatment of carcinoma of the cervix. His final words

"The specific cure for cancer has not yet arrived. . . . Till then surgery and radiotherapy alike are makeshifts—a humbling thought and one which should discourage the acrimony which has crept into their rival claims."

are a salutary reminder of the problem as it still exists, and a challenge to all who are entrusted with the care of these unfortunate patients. In his prophetic Hunterian lecture in 1930, in which reference was made to the future importance of the atom, Mr. Bonney said: "I deprecate as altogether premature the appeals which have been made to the younger gynæcological surgeons not to embark on the operative treatment of

1. Rickes, E. L., Brink, N. G., Koniusky, F. R., Wood, T. R., Folkers, K. *Science*, 1948, **108**, 634.

Digitized by Google

cancer of the cervix, but instead to take up radium therapy." The passing years are proving the wisdom of this protest, and many of those younger surgeons, whom he has trained, are finding that with hands less skilful than the hands which taught them they are able to perform the Bonney-Wertheim hysterectomy with a very low mortality. These results are made possible by team-work, improved anæsthesia, specific chemotherapy, and improvements in preoperative preparation and postoperative care.

In that same Hunterian lecture Mr. Bonney stated that "the truth of the matter probably is that in certain cases surgery, and in others radium, would give the best chance of cure." Believing that until a specific cure for cancer was found the hope for the future, as far as carcinoma of the cervix was concerned, rested in a closer combination of *both* radiation and surgery, I have in my department advocated and practised the Bonney-Wertheim operation, after a full Stockholm course of radium, on suitable cases. That this procedure is logical will be explained in a subsequent publication giving details of the series, which though small is now growing more rapidly. To date only 20 patients have been treated in this way. There have been no operative or postoperative deaths, no fistulæ, and no serious complications. Moreover the fact has been established that if the operation is performed a week after the last application of radium no technical difficulties result from the preliminary radiation. At the follow-up clinic these patients are unbelievably well six weeks after the operation. It is too early to assess end-results, but if they prove encouraging it is to be hoped that with the regional development of medicine patients with cancer of the cervix will be given the benefit of treatment in departments where radiotherapists and gynæcological surgeons, trained to perform the necessary radical surgery, will work in the closest harmony.

If future results justify the combined method of treatment, and by so doing bring life and health to many at present condemned to die, it must not be forgotten that the man who made these results possible by his courageous and brilliant pioneer work was Mr. Victor Bonney, a British surgeon, an international teacher, and a supreme master of surgical technique.

Oxford. JOHN STALLWORTHY.

DEATHS FROM VAGAL INHIBITION

SIR,—The interesting article of April 2 by Dr. Keith Simpson recalled an incident many years ago in a country district in the East when one of the spectators of my treatment of a man who had fainted was a Japanese instructor in jujitsu. This man afterwards demonstrated to me the technique he taught of reviving a man who had apparently been killed by a blow used in this method of fighting.

The blow in question was delivered with the ulnar border of the hand against the opponent's neck to the side of the larynx; I forget which side was considered the most effective. If the blow was successful and it was considered politic to restore the man to life, he was instantly seized by the shoulders and pulled into a sitting posture with his back to the operator, who at the same instant gave him a hard blow with his knee in the region of the 2nd–6th thoracic vertebræ. If no signs of life appeared immediately, the two hands were rapidly placed below the victim's breasts, the skin was gripped with the fingers, and a sudden jerk made as if to tear the skin apart, at about the same time giving a hard kick with the side of the foot just above the sacrum. The instructor used his internal malleolus with as much force as he could muster in his cramped position.

Maybe, as these deaths so often happen in places where no drugs or other means of resuscitation are available, and any treatment to be effective must be given within a matter of half-seconds, someone might like to try this necrologic operation, which can at least do no further harm.

The Japanese method is, I think, preferable to another that I once encountered, which was taught in a primitive community; the instructions were to grasp the testicles of the patient and pull them with a sudden jerk. Unfortunately I cannot speak from personal experience for the effectiveness of either of these two methods, because in the deaths from vagal inhibition I have been called to see, death had always taken place long before I saw the body.

London, S.W.1. R. BRUNEL HAWES.

CARDIOSPASM

SIR,—With reference to the article by Sir Adolphe Abrahams (April 2) and Dr. Magonet's letter (April 9), I suggest that difficulty in swallowing from emotional causes has no relation to cardiospasm but is due to cricoideus spasm—a condition I described some years ago.[1]

The dysphagia of disappointment or sorrow can be extremely severe. I remember well a young mother who had been unable to take any solids for a week. The sight of her infant gave me a clue, and I soon discovered that the source of her distress was that she wanted a boy and had got a girl! The symptoms cleared up almost at once, though I have not heard whether she was luckier next time. In my experience it is not necessary to hypnotise these patients to make a diagnosis. Treatment is less easy, especially where the source of trouble is beyond the patients' control; but in most cases, once they have got rid of the fear of cancer, they learn to disregard the symptom until it disappears.

Bristol. E. WATSON-WILLIAMS.

TUBERCULOUS ABSCESS AT THE SITE OF INJECTIONS

SIR,—Dr. Elek, writing in your issue of April 9, bases his argument against the hæmatogenous origin of tuberculous abscesses following penicillin injections on the failure to discover other tuberculous lesions in the few cases so far reported.

By a coincidence I have, through the courtesy of Mr. C. H. Gray, just seen an instance of a similar condition, although penicillin was not used.

The patient, a married woman of 34, received last December an injection of 'Novutox' into the left buttock for sciatic pain. Two weeks later she sustained an accidental blow on the site of the injection, and this was followed two days later by a swelling at the injection site. She was admitted to Wellhouse Hospital under the care of Mr. Gray, who found a gluteal abscess with much brawny induration and a flexion deformity of the left hip. The abscess was incised and found to be a typical tuberculous abscess. I was asked to see her and found that although she had no chest symptoms, there was, in fact, a lesion in the chest. X-ray examination revealed bilateral infiltration, probably active, with calcified lesions at the left apex.

In my opinion, there is no doubt that this patient, who is suffering from hæmatogenous pulmonary tuberculosis, developed a tuberculous abscess of buttock by hæmatogenous infection of a *locus minoris resistentiæ*, thus supporting the view I have previously maintained in your columns (*Lancet*, 1946, ii, 617).

Clare Hall Hospital, South Mimms, Barnet. A. G. HOUNSLOW.

THE UNDESCENDED TESTICLE

SIR,—Many years ago, when I asked an eminent physicist why the F.R.S. was never given for clinical work, he replied: "You doctors don't discuss like scientists: you dispute like theologians." The remark stung and it stuck; I have had more and more to admit to its justice. Consider Dr. Simpson's statement (April 2): "Clinical diagnosis can be sound whether or not his new anatomy should replace the older." This is very like much theological argument, but can anyone imagine a chemist saying "My results are sound, whether or not the substances I was working with were what I thought them to be"?

The letters from Dr. Simpson and Dr. Spence (April 9) express very well the almost invariable reaction of anatomists, surgeons, and physicians to the half-dozen papers I have published querying the correctness or the completeness of the sacred books of anatomy. No professor, no senior surgeon, and no physician has ever come to me to say "This is interesting: can you really

1. A Lump in the Throat. *Bristol med.-chir. J.* 1937, **54**, 279.

Digitized by Google

prove it?" On the contrary, my first statements are ignored, and my repetition of them is met by the complaint that I am becoming a bore by repeating myself.

The argument is essentially anatomical, and the trouble is that anatomy is bound by two rigid fetters: the examination system and the dissecting-room. The first means that it is unfair to one's students to teach them unorthodox anatomy when they may be examined by an orthodox professor. Hence a further resemblance to the theological atmosphere: not a few of my young men have found themselves in examinations faced with the choice of making a very risky statement which they consider true; or of parroting orthodox textbook anatomy which they consider false. The anatomical limitations of the dissecting-room are even worse. The young do not come there, and the material of study lies stiff and motionless.

Dr. Spence's claim that endocrinologists carefully examine and classify their cases is meaningless unless he states what classification is used. He cannot use mine as, if correct, it destroys his work; I know of no other. His carrying of an opinion I do not hold to its "logical and ridiculous conclusion" is hardly scientific discussion, and his last paragraph is so loaded with sarcasm that I am unsure of its meaning. But if this is that no substances naturally found in the body can be harmful, he should consider the adrenal and the thyroid secretions.

In this business of undescended testicles I still occasionally find diagnosis extremely difficult; I am still learning; and I still make mistakes. But I am, I honestly think, a long way ahead of those who consider that the testicles they feel above the pubis are in the inguinal canal. And all endocrinologists whose papers I have read do this.

London, W.1. DENIS BROWNE.

TRAINING OF HEALTH VISITORS

SIR,—The proposals on the training of health visitors discussed in your annotation of April 2, merit careful thought. Dr. Davies and Dr. Brockington are right in emphasising the importance of the health visitor and the need for ensuring that her training and qualification command general respect.

There is no doubt that she can be employed to further efforts by local authorities in the prevention of illness under section 28 of the Act. To suggest, however, that this, or her duties under section 24, necessitates that three-quarters or more of the time spent in her specialised training should be devoted to a social-science course equally suited to almoners and industrial nurses, seems to me quite unjustifiable. The health visitor is primarily a health educator working among mothers —an adviser, "the counsellor of motherhood." She is secondarily an agent for social amelioration; and thirdly an agent for "intelligence" on behalf of the health department.

Rearing healthy children is still the most important work in the world, and it would be a very rash individual who would suggest there are not still fields to be explored in the achievement of health in childhood and adolescence. The health visitor's influence is due to her being able, by her experience in nursing and midwifery, to give helpful advice to a mother, at a most impressionable stage, on the subject of her greatest concern. The influence of any outsider on the family as a whole is related to, and mainly due to, her influence with the mother. It is not, and never will be, due to any profound knowledge of social science, of economic theory and practice, of legal enactments, and the like. No-one will deny that a knowledge of modern social legislation, of public and voluntary social services, and of the technique of case conference is necessary to a health visitor. But the practical care of the child within the family, the economics and technique of household management, the psychology of childhood and adolescence, the normal physical and mental levels in young life, maturity, and senescence, and the methods of individual and group teaching in the field, are, it seems to me, still the fundamentals in the health visitor's training. She is still a personal health worker.

Let the health visitor's training and examination remain specialised. Let us encourage entrants with maturity and yet initiative, knowledgeable in human experience and suffering, familiar with the evidences of sickness and health, able to advise with authority and to help with sympathy. As regards training, adequate experience of midwifery (on the district) is necessary if the health visitor is to be able to share, even in a limited way, in the mother's experience, and to appreciate what the newborn baby means to the mother and the mother to the babe. The specialised six-month course seems too crowded; and if it be necessary to have a university training *and* diploma, they should be afforded under the ægis of the department of preventive or social medicine—what we seek is the ideals and background of medicine informed by social science. I doubt the need for the university diploma.

My own views published in *Mother and Child* (1943) have changed somewhat, particularly in view of the proposals made by the nurses' working party. Most will agree that an extension in the duration and content of the health visitor's training, especially in relation to social work, is necessary, but I am convinced from close knowledge of the work of health visitors that the proposals of Dr. Davies and Dr. Brockington require considerable modification.

Dewsbury. E. D. IRVINE
Medical Officer of Health.

CORONARY THROMBOSIS

SIR,—I was much interested in the letter from Dr. Snowman in your issue of April 2. As a general practitioner I too have once or twice seen death follow rapidly after the administration of morphine in the acute stage of cardiac infarction, but cardiologists appear to doubt that the drug has any part in the fatal outcome. I would suggest, however, that in a condition of acute shock morphine, by producing a further fall of blood-pressure, might tip the scales against the patient.

In my experience aminophylline is a much safer drug to employ in the acute stage of the disease; it appears to be almost as effective in relieving the patient's distress, particularly if pulmonary œdema and bronchospasm are associated as manifestations of left-ventricular failure. My practice is to give 0·5 g. of the drug intramuscularly or (well diluted and very slowly) intravenously. I would suggest that this drug be given as soon as the diagnosis is made, and that morphine be given if necessary later, when the initial shock has passed off to some extent.

Birmingham. H. JOSEPHS.

SPECIALIST QUALIFICATIONS

SIR,—The leader in your issue of Jan. 8, which has just reached here, demonstrates a number of the faults of the present British system, but fails, I feel, to point out others.

In the greater part of the British Empire the medical degrees of the many universities and the diplomas of the Royal Colleges or similar institutions are recognised as suitable for registration without further examination. This system is greatly superior to that of France, for example, where university graduates are compelled to take the State examination and consequently must all be coached on an identical standard. The British qualifications have a uniform level which nevertheless permits individuality and local emphasis.

This cast-iron standardisation of the French is, to a large extent, avoided in America by each State having its own registration examination, with a wide degree of reciprocity.

It is unfortunate that at the specialist level British medicine is developing its own bottleneck. At this level the high qualifications of the various examining boards are no longer looked upon as different but roughly equivalent, but the Royal Colleges have almost succeeded in laying down that they alone can issue licences for specialist appointments. This state of affairs is distressing firstly because it gives a grossly unfair advantage to those who, in the junior years, have not the enterprise to move far from the coaching and examining centres, and secondly because it tends to convert British postgraduate teaching into a series of cram classes. Both in India and here I have been distressed to see that the young graduate goes to Britain to collect postgraduate diplomas and goes to America to learn the recent advances

Digitized by Google

in his subject. It would be far better if he aimed at the higher degree of his local university and went overseas to widen his mind both professionally and generally. May it not be that the greatest advances are being made in bacteriology and pathology because there is no generally recognised postgraduate diploma in these subjects?

To the suggestion that the F.R.C.S. be made "much more difficult" I ask "What is wrong with the present holders of that diploma?" Is it not obvious that all too often high examinations are not being used as a test for knowledge or skill but as a means for keeping the other fellow out?

Nelson, New Zealand. R. L. HAVILAND MINCHIN.

AT THE CROSS-ROADS

SIR,—I am most interested in the letter from "Veritas" (April 9). To avoid any possibility of controversy may I explain that if space had permitted I should have given the references on which my lecture was based. It was my intention in that lecture to review the development of our health services, and to this end I consulted first Dr. J. F. Payne's scholarly lectures on English Medicine in Anglo-Saxon times. These two FitzPatrick lectures were delivered before the Royal College of Physicians of London in 1903. Dr. Payne, a former fellow of Magdalen College, Oxford, and consulting physician to St. Thomas's Hospital, was at that time Harveian librarian of the College of Physicians. On p. 12 of his lectures he says that "the beginning of learning and civilisation in a strict sense among the Anglo-Saxons cannot be dated earlier than the introduction of Christianity by Augustine in A.D. 597."

Ministry of Health, London, S.W.1. A. LESLIE BANKS.

CONGESTIVE HEART-FAILURE

SIR,—I must congratulate Dr. Reid and Dr. Hughes on their excellent article of April 9. I should like to ask however whether they have checked the plasma-protein level in cases with persistent œdema and a good urinary output who are given regular mersalyl and a low-salt diet? I remember one case in the last year where a plasma-protein content of 4·5 g. per 100 ml. could not be explained by the raised blood-volume. It increased to normal very rapidly, however, with a diet containing 140 g. of protein a day for a short period. The prolonged asthenia in some of these cases may well be due to a low plasma-protein figure when the low-salt diet and mercurial diuretic and digoxin have been all too efficient in controlling the manifestations of congestive failure.

Jewish unleavened bread, which is salt-free, is a welcome alternative to many patients, as are 'Energen' bread and rolls.

Langthorne Hospital, London, E.11. L. COSIN.

CLINICAL ESTIMATION OF BASAL METABOLIC RATE

SIR,—My replies to Dr. Bene's letter last week are:

1. An indicator is misnamed if it fails to indicate.
2. No.
3. How in the name of du Bois can the B.M.R. be "in no way related to heat output"? Dr. Bene's paper was called "the Clinical Estimation of the Basal Metabolic Rate."
4. I agree that these cases were unusual. Most cases of thyrotoxicosis are unusual. The versatility of the disease makes any simple formula look silly.
5. I agree that insistence on only 5 minutes' rest makes a lot of difference. Dr. Bene's method would show every athlete to be thyrotoxic after a run.

Penultimate paragraph: (*a*) See 4 above. (*b*) Dr. Bene misunderstood me. The B.M.R. is useful only in a few cases because it is seldom necessary, not because it is inaccurate.

Ultimate paragraph: (*a*) There is no contradiction; see last paragraph. (*b*) The fact that Read and Boothby presumed the practical usefulness of their formulæ does not alter the fact that they are useless.

To sum up, the diagnosis of thyrotoxicosis can almost always be made with certainty on clinical grounds alone. No oversimplified formula can approach in accuracy the evidence of the senses. In the rare cases in which the physical signs are confusing, the B.M.R. is accurate and helpful. The instances I have quoted show that the R.P. index is not. No-one acquainted with the wild heterodoxy of thyrotoxicosis would expect it to be.

From this source at any rate, Sir, this correspondence will now cease.

RAYMOND GREENE.

Thyroid Clinic, New End Hospital, London, N.W.3.

RETROPUBIC PROSTATECTOMY

SIR,—The letters from Mr. Chapman (March 19) and Mr. Vernon (March 26) would seem to most to call for no reply. Surely it is commonplace knowledge that not all enlarging prostates progress at the same rate, and that many patients with minimal symptoms can be safely watched. Mr. Chapman says that it is his practice "to treat expectantly all patients with prostatic enlargement and only a small quantity of residual urine, unless difficulty in micturition is *very extreme*." It would seem to us little comfort to the patient who seeks relief regarding severe prostatic symptomatology to be told that his case does not fulfil certain criteria, such as the obsolete residual-urine test advocated by both your correspondents. For example, they cannot but be aware that the large extravesical lateral-lobe hypertrophies, well known to cause extreme symptomatology with perhaps upper-tract dilatation and renal insufficiency, may be associated with minimal or absent residual urine. Are they going to deny surgical relief to such a case merely because it fails to satisfy their criterion? If so that patient is going to seek advice elsewhere, as we well know.

No, Sir, Mr. Vernon's epic sentence hailing the presence of *residual urine* as the "*sheet anchor*" of prostatic surgery (surely one of the most remarkable examples of mixed metaphor in surgical literature) seeks to perpetuate an archaic teaching long abandoned by most urologists.

The point we wished to make in our article, backed by mortality figures, was that with modern methods it is better to operate early rather than late, or, at worst, too late, always provided that we are satisfied that the lesion is progressive and that symptomatology warrants interference. In our article of March 5 we designedly used the term *established* prostatic obstruction.

TERENCE MILLIN
London, S.W.7. C. L. O. MACALISTER.

KWASHIORKOR

SIR,—May I be permitted to return to the terminological battle? In a leading article on Jan. 29 you quote Dr. Trowell as stating that the rash in kwashiorkor is pellagrous though not necessarily a feature of the disease.

When the word kwashiorkor made its début in print in your pages I tried to point out the differences between this condition and pellagra[1]:

Kwashiorkor	*Pellagra*
Affected skin black, rugose, and soft.	Affected skin rough, dry, and branny.
Extensor surfaces and points of irritation and pressure affected.	Face, necklace area, and dorsum of hands and feet affected.
Skin not photosensitive.	Skin photosensitive.
Occurs in children under five years.	Rare in children.
Usual under two years.	Almost unknown under two years.
Reflexes unchanged.	Peripheral neuritis common.
Dementia not observed.	Dementia common.
Patients may be largely on a breast-milk diet.	Very rare with milk diet.
Arkasa (preparation of maize) in diet contains yeast.	Yeasts said to be curative.
Fatty infiltration of liver severe and constant.	Fatty infiltration of liver may be present, but is generally mild.
Never seen in adults.	Common in adults.
Common condition in the Gold Coast.	Never yet described in the Gold Coast.

I should have added that whereas kwashiorkor is frequently fatal, pellagra is rarely so. Otherwise the differentiation still stands fairly good.

It is not easy to describe differences in skin conditions, but before this rash is again called "pellagrous" I would like to point out some of the puzzling questions.

1. *Lancet*, 1935, ii, 1151.

Digitized by Google

Kwashiorkor is common, and seems to be getting more common, in Africa, even among the relatively well-nourished Gold Coast population. It is seen also in the West Indies, but is rare in India. In Budapest they tell me it was common during and immediately after the war. In twelve years in Malaya I saw only 2 typical cases. (One was in a Chinese boy who ultimately died of tuberculosis, and who, according to the history, had been on a good diet.[2] The other was in a Eurasian child of two years who was admitted to an internment camp in 1945 and who ultimately made a good recovery. I saw him in 1947 looking well and strong.) Yet cases of malnutrition were on the whole very much more common in Malaya than in West Africa, and the different races there represented differed widely in their food habits. The races well represented were Malays, Chinese, Tamils, Bengalis, Sikhs, Europeans, Ceylonese, and Javanese; and the foodstuffs available were very much the same as those in West Africa.

Nutritional disturbances produce a variety of skin appearances. Besides the typical appearances of certain well-marked conditions there is an infinite range of intermediate and mixed conditions. I still maintain that a typical kwashiorkor is so different from a typical pellagra that it is quite impossible to confuse the two conditions; and I never saw a true, pure, typical pellagra in the Gold Coast. Nor had anyone else until they started to call kwashiorkor "infantile pellagra."

During internment in Singapore we saw many cases of acute pellagra. They were always the same. The skin that was exposed to sunlight, and nowhere else, became swollen, red, and painful, with a well-marked line of demarcation. The redness proceeded to dry, brawny desquamation and even ulceration unless treated or protected. Patients sometimes showed accompanying angular stomatitis, hæmorrhagic blebs, sore tongue, &c.; sometimes not.

In one woman who did a lot of gardening (weeding and stooping in shorts) the rash first appeared at the back of the knees. In another who sat in the sun on the verandah it was on the dorsum of the feet, and so forth. In every case the rash was controlled by protection from the sunlight. (We had no nicotinic acid, and little in the way of supplementary diet.) There has been nothing to suggest that the skin in kwashiorkor is photosensitive. This seems to me a significant difference which is usually ignored.

Geneva. CICELY D. WILLIAMS.

FIBROCYSTIC DISEASE OF THE PANCREAS

SIR,—In his case-report of April 16 Dr. G. G. Jones states that cases in Andersen's group 3 are clinically indistinguishable from cases of cœliac disease. This is not so; for, if a careful history is taken, a history of poor weight gain and abnormal stools from early infancy will be obtained in the great majority of cases of fibrocystic disease but not in cases of cœliac disease whose early development is normal. The view that the two diseases are distinguishable clinically is supported by Sheldon.[3] It should also be mentioned that cases in group 3 may present with chronic respiratory infections.

Although it is a reasonable assumption, there is no direct evidence that the cases which live longer are milder examples of the disease.

Peripheral œdema of nutritional origin is not uncommon terminally in untreated cases, and I have seen it on two occasions: in one of these cases a history of peripheral œdema was obtained in 2 of her 3 siblings, all of whom had died before the age of six months of bronchopneumonia and in all of whom the histories were typical of fibrocystic disease. Considering the difficulty in digesting protein which is present, it seems not unreasonable to expect that hypoproteinæmia and œdema will occur.

Although it is true that the pancreas frequently appears normal externally at autopsy, dilated ducts can often be seen naked-eye on cross-section.

Fibrocystic disease of the pancreas is not an uncommon disease and the diagnosis should be considered in all cases of chronic nutritional or respiratory difficulty in children. I believe that with an accurate history the diagnosis can usually be made clinically.

W. J. MATHESON.

Children's Hospital, Royal Infirmary, Leicester.

2. Williams, C. D. *Trans. R. Soc. trop. Med. Hyg.* 1940, **34**, 85.
3. Sheldon, W. *Brit. med. J.* 1948, ii, 594.

RESISTANCE TO PROGUANIL

SIR,—I was interested to read the article by Dr. Seaton and Dr. Lourie in your issue of March 5. They were concerned with acquired resistance to proguanil ('Paludrine') in *Plasmodium vivax* infections; and they concluded that with *P. vivax* there is little danger of this resistance occurring naturally. I should like to draw attention to the occurrence and dangers of naturally resistant strains of *P. falciparum*.

Experience in the Aden Protectorate (and also, it is reported, in the Yemen) shows that paludrine is almost totally useless for the treatment of most cases of M.T. malaria. My own cases have all been in Arabs, who have a well-developed immunity. Even when untreated the disease (reinfections, not relapses) is self-limiting and seldom lasts more than ten days, though a relapse may follow. Treatment with paludrine (300–900 mg. daily) did not seem to affect the temperature or cause the spleen to recede, as quinine did; and relapses took place, even as soon as five days after the end of a course of 3 g.

The danger of such strains to Europeans is obvious if treatment with paludrine alone is persisted in. It is hoped to publish a series of cases shortly, but meanwhile a warning of the limitations of the drug seems timely.

Aden. H. E. M. KAY.

Parliament

The Budget Debate Continued

IN the course of the debate Sir JOHN ANDERSON applauded the Chancellor's statement that we must moderate the speed of our advance in extending the social services to our progressive ability to pay for them. How much better, Sir John declared, if that lesson had been driven home two and a half years ago. On a long view the improved standard of health and education resulting from the development of the social services ought to increase enormously our productive efficiency. But the Government had gone ahead too fast, and instead of developing the social services and building up the economy of the country stage by stage, they had concentrated on increased expenditure without attending to the prerequisite of a sound economy.

The Budget reminded Dr. A. D. D. BROUGHTON of a mixture containing all the essential ingredients for the recovery of the patient, but lacking in carminatives to make it palatable. The Budget had been described as one of harsh realism, he continued, but it was also a monument of courage and integrity. He would be grateful, however, if the Chancellor of the Exchequer would look into the suggestion that old-age pensioners should be allowed to enjoy their food at the previous prices.

Sir HUGH LUCAS-TOOTH said that if the Treasury circular had any effect it must be to hold up the health scheme altogether in some vital part. The current health estimates were quite unreal. The hospitals were expressly told that they were not to take into account any contingency, despite the fact that in any business, hospitals or other, contingencies were bound to arise. After the estimates had been submitted, heavy increases of expenditure were imposed on the hospitals under the Spens Committee's report on additional pay for specialists. After that the hospitals were told that a cut had to be made. These cuts could not possibly be made, and it was no use the Government pretending that by circularising the Department, and saying that supplementary estimates would not be honoured, that that would effect the cuts; it would not. There were only two alternatives: either there would be large supplementary estimates under these headings, or a large number of hospitals would be virtually brought to a standstill. The effect of the duality of policy now being pursued by the two halves of the Government was that

Digitized by Google

they would either break the back of the health services—and probably also most of the other social services of the country—or they would break the back of the Budget.

Medical Care for Foreign Visitors

In the House of Commons on April 8 Sir WALDRON SMITHERS described the National Health Service leaflet no. 2, which he understood was available to all visitors on arrival in this country, as "another bit of evidence of the extravagance, maladministration, and irresponsibility of the Socialist Government." It stated that visitors, whether of British nationality or not, could use the National Health Service, or any complete part of it. Yet the National Health Service Act stated that it should be the duty of the Minister of Health to promote the establishment of a service designed to secure improvement in the physical and mental health of the people of this country. He wished to ask how many copies of this leaflet had been distributed, and at what cost; how many foreigners had taken advantage of these services and at what cost; whether the people of Eire were to be included in this service; and under which section of the Act the leaflet was issued.

Dr. HADEN GUEST asked if there was any evidence that people were coming to this country and spending their time having dentures, wigs, artificial legs, and so on fitted on anything like a large scale. Mr. WILLIAM SHEPHERD agreed that visitors would not be able to take much advantage of the facilities offered in respect of the supply of teeth, wigs, and spectacles because they would have to stay so long that their expenses would outweigh any material advantage gained, but at the same time, he held, the House of Commons was entitled to take note of the complaint. What advantage was there in bringing these facilities to the notice of foreign visitors? He suggested that this was an excess of zeal on the part of the Minister or some of his officials.

Mr. KENNETH LINDSAY, on the other hand, thought it an excellent idea, and wanted to see the Minister make this service reciprocal. If we meant anything by Western Union, he suggested, we had to extend it not only to the economic field but to the whole of the social services.

Mr. ARTHUR BLENKINSOP, parliamentary secretary to the Ministry of Health, held that one of the virtues of the National Health scheme was that it involved little red tape and form-filling for the patient. It would mean masses of red tape and a great deal of new organisation if we were to try to discriminate in a highly undesirable way between one section of people in this country and another. There was no question at all about the legality of the leaflet. The Act covered the position completely. In all 750,000 copies of the leaflet had been printed, and up to date 170,000 had been distributed. Figures could not be given of the number of foreigners who had been treated under the Act because to obtain them it would be necessary to complete some difficult forms and examinations in regard to nationality which were undesirable. Americans, Canadians, and others who had come to our shores had expressed themselves as delighted and gratified with what we were able to do for them. Last year, Mr. Blenkinsop ended, approximately 633,000 foreign visitors came to this country. If they stayed about a month and were to make the average use of the services which the ordinary population enjoyed—which was highly unlikely—the cost would be something like £200,000 a year. He did not think that that should arouse any anxieties in this country.

QUESTION TIME

Pension Claims for Hodgkin's Disease

Sir GIFFORD FOX asked the Minister of Pensions how many claimants suffering from Hodgkin's disease applying for pensions were awaiting the rehearing by the pensions appeal tribunal of the test case resubmitted to them by the nominated judge of the High Court dealing with these appeals; and when was a decision likely to be given.—Mr. H. A. MARQUAND replied: The number of claimants whose appeals are awaiting the outcome of the two test cases remitted to the pensions appeal tribunal by the nominated judge of the High Court is 172. One case has been heard recently by a pensions appeal tribunal and disallowed; the other is expected to be heard next month. When the tribunal decision in the second test case becomes available a pronouncement by the learned judge will be sought at the earliest possible date.

Fats in the Rations

Mr. RUPERT DE LA BÈRE asked the Minister of Food, as leading medical authorities attributed the tiredness and apathy of large sections of the public today to the fact that these people were getting a diet with insufficient animal fats, what steps he was taking to remedy this as far as practicable by providing additional quantities and varieties of other commodities to take their place.—Dr. EDITH SUMMERSKILL replied: The Economic Survey for 1949 estimates that total fat-supplies (including animal fats) will be some 5% higher and supplies of fat sold in the form of fat (including butter), some 12% higher in 1948–49 than in the previous twelve months. But naturally we are doing all we can to improve supplies still further.

Child Care

Mrs. M. E. NICHOL asked the Home Secretary what progress had been made since the publication of the Curtis report in transferring to better accommodation children living in former public-assistance institutions.—Mr. CHUTER EDE replied: When the Curtis Committee reported in 1946 it was estimated that 6500 children were living in public-assistance institutions. According to the latest returns the number of children in care under the Children Act, who are in accommodation provided under the National Assistance Act, is now about 1600.

Dressings for Maternity Cases

Dr. L. COMYNS asked the Minister of Health where expectant mothers attending antenatal clinics should obtain maternity packs and dressings for the lying-in period; if he was aware that the West Ham local authority is refusing to issue such free packs and dressings, and that expectant mothers are referred to their general practitioners for the sterile dressings, &c.; and whether it was in order for practitioners to issue such prescriptions.—Mr. ANEURIN BEVAN replied: Local health authorities should arrange for maternity outfits for domiciliary confinements to be supplied at clinics, through midwives, or in some other convenient way, and for other dressings required during the lying-in period to be provided by the midwife in attendance. I understand that the West Ham council are at once reconsidering their practice. Maternity outfits and sterilised dressings are not included in the schedule of appliances which a general practitioner may prescribe for his National Health Service patients.

Hospital Beds

Replying to a question Mr. BEVAN stated that between June 30 and Dec. 31, 1948, the increase in the number of staffed beds in general hospitals in England and Wales was 15,510.

Marriage Guidance Councils

Mrs. BARBARA CASTLE asked the Secretary of State for the Home Department whether, in the light of the recommendations of the Harris Committee, he was yet in a position to make a statement on the grant-aiding of local marriage guidance councils.—Mr. CHUTER EDE replied: Under section 136 of the Local Government Act, 1948, a local authority can, subject to the consent of the Minister of Health, contribute towards the expenses of a local marriage guidance council. Having regard to the general arrangements for Exchequer assistance to local authorities, H.M. Government do not propose to adopt the recommendation of the departmental committee, that half the expenditure so incurred by a local authority should be met by a special Government grant. I propose to ask the House to authorise for the current financial year the expenditure recommended by the departmental committee on grants towards the headquarters expenses of the National Marriage Guidance Council, the Catholic Marriage Advisory Council, and the Family Welfare Association, and also on selection and training of marriage guidance counsellors by a body which I propose to set up for that purpose.

Mr. A. M. SKEFFINGTON-LODGE: Can the Minister say what type of person is serving on these marriage guidance councils; and has he any control over the nomination of people to serve on them?—Mr. EDE: On the whole these people are doing quite good public service in this connexion, and I should hesitate myself to act as a censor.

Digitized by Google

Public Health

RESPIRATORY MORTALITY AND MORBIDITY IN LONDON

G. E. BREEN
M.D. N.U.I., D.P.H.
EPIDEMIOLOGIST

B. BENJAMIN
B.Sc. Lond., F.I.A.
STATISTICIAN

PUBLIC HEALTH DEPARTMENT, LONDON COUNTY COUNCIL

THE occurrence of widespread outbreaks of influenza on the Continent at the end of last year, reaching a peak in France about the end of December, and the threat of extension of the epidemic to this country, led public-health authorities to take special preparatory measures. All services were alerted so that maximum deployment could be made. In the event the epidemic did not materialise on the scale expected. The exact extent is not precisely known, but available evidence suggests that while it was widespread in some areas, in others it was scarcely appreciable. The statistics for London are given in the accompanying table.

RESPIRATORY DISORDERS AND AIR-TEMPERATURE AND FOG IN LONDON DURING THE FIRST TWELVE WEEKS OF 1949

Week ended	No. of deaths registered			No. of cases removed to hospital by London ambulance service		Air-temperature at Greenwich, mean daily value, degrees Fahrenheit	Fog	
	Bronchitis	Influenza	Pneumonia	Influenza or influenzal pneumonia	Pneumonia		Date	Duration, hours
Jan. 8	91	6	75	not available		41·8	Jan. 8	..
,, 15	108	8	53	16	122	42·0	,, 10	2
							,, 15	12
,, 22	93	3	51	4	163	46·0	,, 22	11½
,, 29	89	6	52	4	123	42·2	,, 26	5
							,, 27	18½
							,, 28	5
							,, 29	"foggy"
Feb. 5	150	13	70	37	147	35·5	,, 30	24
							,, 31	12
							Feb. 2	5
							,, 4	15
,, 12	215	11	98	27	197	40·9	,, 5	13
							,, 6	5
							,, 10	5
							,, 11	mist or fog throughout day
,, 19	212	33	104	63	229	46·0	,, 19	3
,, 26	155	40	105	21	239	47·6	,, 20	morning mist 5
							,, 24	mist and high fog in morning
							,, 25	6
March 5	137	48	75	30	178	38·2	,, 28	high fog 7
							March 3	high fog 1
							,, 4	4
,, 12	139	39	83	17	165	35·9	,, 11	1
							,, 12	..
,, 19	101	31	71	18	128	44·5	,, 19	mist 6
,, 26	79	26	62	10	125	47·1	,, 20	3½
							,, 21	5
							,, 22	mist 6
							,, 25	

The total deaths in London from bronchitis, pneumonia, and influenza in the first twelve weeks of 1949 numbered 2732 compared with 1487 in 1948 (a notably light year), and 3369 in 1947 (a year of heavy respiratory mortality with severe winter conditions). Influenza was the registered cause in 264 deaths this year, compared with 39 in 1948, and 210 in 1947; and it would therefore appear that there has been an increase in influenza mortality, though not on the scale of the last major outbreak in 1937, when in the 13-week period ended March 13 there were 1482 influenza deaths. On the whole, however, these figures mainly indicate an expected exacerbation of respiratory morbidity by winter conditions.

The correlation between respiratory mortality and both temperature and fog has been examined by Russell [1] and Woods.[2] The general impression is that temperature is the dominant factor and fog normally only a minor factor, but that the combination of fog with low temperature is particularly likely to produce high respiratory mortality. This has recently been illustrated for London by Logan.[3] The table shows that the week ended Feb. 5 was marked by an upward turn in respiratory mortality and hospital admissions. In this week the mean temperature was low and there was a considerable amount of fog. There was a rise in temperature and reduced frequency of fog in the week ended Feb. 19, after which the mortality and morbidity remained high for only one further week and then began to fall. The influenza mortality did not reach its peak until two weeks later, indicating that in addition to the effect of winter conditions there was an increased level of infection.

Smallpox in England and Wales

As previously reported, a passenger on S.S. *Mooltan* sickened on March 21, developed a confluent rash on March 25, and died at sea on April 1. In England and Wales, up to last Monday, secondary cases had been reported at the following places:

	Onset of illness April
Port of London	3
Paddington	5
St. Pancras	5
Isle of Axholme	5
Paddington	6
Liverpool	6
Wembley	7
Sutton and Cheam	7
Torquay	8
Aylesbury	12
Richmond	12

There remains some uncertainty concerning the diagnosis in cases reported from Southwark and Abertillery, Wales. In numerous other people who travelled on S.S. *Mooltan*, and who have subsequently come under medical observation, suspicion of smallpox has not been confirmed.

All the confirmed cases listed in the table had been in contact on the S.S. *Mooltan*; so far no cases infected in this country have been reported, but these are expected to appear at any time. The disease is a severe form of variola major; 5 of the patients have died, 2 in the prodromal phase. In some the disease has been hæmorrhagic; in others there is extreme modification resulting from vaccination.

Two patients are under observation at the Laceby Smallpox Hospital, Lincolnshire. They are in no way associated with the S.S. *Mooltan*, and furthermore the diagnosis is uncertain. They come from Brigg and Bolton-on-Dearne and sickened on April 13 and 14 respectively.

Population Estimates for 1948

In a new publication [4] the Registrar-General shows his latest estimates of the civilian population of each area in England and Wales. This publication is designed to meet the demand for an early issue of up-to-date figures of local populations before these appear in the annual statistical review.

As already announced (see *Lancet*, April 9, p. 633), the total population of England and Wales at June 30, 1948, is estimated at 43,502,000. The civilian population of Greater London is given as 8,282,217, and of the administrative county of London as 3,339,100. Birmingham is the next largest with 1,096,100. The total population at Dec. 31 is estimated at 43,676,000.

1. Russell, W. T. *Lancet*, 1924, ii, 335; *Ibid*, 1926, ii, 1128.
2. Woods, H. M. *Ibid*, 1928, i, 539.
3. Logan, W. P. D. *Ibid*, Jan. 8, p. 78.
4. Registrar-General's Estimates of the Population of England and Wales. H.M. Stationery Office. Pp. 15. 4d.

Digitized by Google

Obituary

DONALD GEORGE HALL

M.A., M.D. CAMB., F.R.C.P.

Dr. Donald Hall, consulting physician to the Royal Sussex County Hospital, Brighton, died on April 8 at the age of 72.

Born at Gatehouse-of-Fleet, Kirkcudbrightshire, he was educated at Edinburgh Academy and Emmanuel College, Cambridge, where he held a scholarship and captained the rugby XV. In 1897 he graduated with first-class honours in the natural sciences tripos. He returned to Edinburgh for his clinical work, and, after graduating as M.B. Camb. in 1900, was house-physician, at the Royal Infirmary and Royal Hospital for Sick Children in Edinburgh. Soon after he qualified, smallpox broke out in his stepfather's practice at Gatehouse-of-Fleet. Characteristically he went home and took charge of the smallpox cases, for which he received a grateful presentation from the other patients of the practice, who had been afraid of the spread of the infection.

[Polyfoto

In 1904 he went to Brighton as house-physician to the Royal Sussex County Hospital, and he spent the rest of his life in its service as assistant physician, physician, consulting physician, chairman of the board of management and standing executive committee (1938–45), and finally as president. Especially notable was his chairmanship during the war years, for his administrative ability was as invaluable as his patience and good temper.

Dr. Hall played his part in three wars. He was surgeon in the hospital ship *Nubia* in the South African war and a major in the R.A.M.C. with the second South-Eastern General Hospital in 1914–18; and during the late war he returned to active work at the Royal Sussex County Hospital, which served naval, military, and R.A.F. establishments as well as the civilian population and air-raid casualties.

He was in general practice in Brighton and Hove until 1923 when he became a fellow of the Royal College of Physicians. From that time he built up a large consulting practice. Though he was a pioneer in the treatment of pulmonary tuberculosis by artificial pneumothorax, cardiology became his main interest. As early as 1924 he read a paper on the use of the electrocardiograph, and his work in this specialty was later recognised by his election as chairman of the Cardiological Society of Great Britain.

His connexion with the Brighton and Sussex Medico-Chirurgical Society was long and useful; he joined it in 1905, was president in 1927, and was honorary librarian from 1922 until his death. He read many papers before the society, mainly on cardiological subjects; fellow-members will recall, for example, his address on cardiac pain in 1930 when he persistently pronounced angina correctly with a short "i." His last paper, in 1943, on cardiac curiosities, was a masterly exposition of his wide clinical knowledge. He was president of the Sussex branch of the British Medical Association, on whose ethical committee he served as chairman. He was also a justice of the peace for the borough of Hove. A first-class fisherman and a good shot, he went regularly to Scotland where he entertained his friends with excellent sport and true Scottish hospitality.

G. M. W. writes: "In physical appearance, Donald Hall was upright and stocky; his open-air aspect and springy step gave the impression of a great reserve of strength. His academic distinction and administrative ability were the result of hard work based on a powerful brain; he showed no sign of effort or strain, but he seemed naturally to rise to all occasions, and thus came to be accepted as a leader in all medical matters. As a clinician his reputation was unrivalled. He was a sound and reliable diagnostician and his advice was wise and practical.

"A modest man, he never lifted a finger in his own interest, and he was a real democrat, taking a friendly interest in all his friends, among whom he counted every porter and cleaner at the hospital, as well as the residents, sisters, nurses, and his colleagues. There can be hardly a doctor in Sussex who does not remember Donald Hall's kindness."

Like many other physicians, Dr. Hall died of a disease which he had made a special study—coronary occlusion. There was no warning, and no failing in mind or body.

MAURICE SORSBY

M.D. LEEDS, F.R.C.S.E.

Dr. Maurice Sorsby, who died at Los Angeles on April 6 at the age of 50, graduated at Leeds University in 1922, proceeding to the M.D. degree in 1925. In the same year he also obtained the F.R.C.S.E. Coming to London he chose otolaryngology as his specialty, and he held staff appointments at the Metropolitan Ear, Nose, and Throat Hospital, the London Jewish Hospital, and the Plaistow Children's Hospital. He was also for a time consulting ear, nose, and throat surgeon to the London County Council hospitals. His early training in general surgery turned his interest mainly to the intracranial complications of ear disease, and to the general aspects of the cancer problem. In his monograph *Cancer and Race*, which was published in 1931, he described his detailed study on the incidence of cancer in Jewish communities in different parts of the world, from which he concluded that the total cancer-rate in Jews was everywhere approximately the same as that in the general population, though the distribution according to organ varied considerably. The variation could often be explained by environmental factors: for instance, the low incidence of cancer of the tongue could be correlated with a low incidence of syphilitic leucoplakia, which so often precedes it. Sorsby's study on Beethoven's deafness was characteristic of his wide interests, and a busy professional career still left him time for social activity. As a president of the London Jewish Hospital Medical Society he was largely instrumental, together with the late Dr. M. D. Eder, in forming the Emergency Medical and Dental Association for the relief of victims of Nazi persecution. His wife survives him with two sons.

FELIX D'HERELLE

M.D. MONTREAL

Professor d'Herelle, who died in Paris on Feb. 2, was best known for his work on bacteriophage. He was born at Montreal in 1873 of French-Canadian parents, and though he retained his British nationality he gave the impression of being less British than French in temperament and outlook. Educated at the Lycée Louis le Grand, Paris, he took his baccalaureat in 1888 and then returned to Canada to take up the study of medicine and to graduate M.D. Montreal. From 1901 to 1906 he held the chair of bacteriology at Guatemala, and in 1907 he was appointed bacteriologist to the Mexican government. In the following year he went to Paris as assistant at the Pasteur Institute, where he was later chef de laboratoire from 1914 to 1921. At the request of governments he undertook missions to the Argentine (1911–13), Turkey (1914), Tunis (1915), and Indo-China (1921). In 1921 he went to Leyden as professor extraordinary, and two years later was appointed to the International Sanitary Council, Egypt, as director of the bacteriological service. There he remained until 1926, when he visited India on a special mission at the request of the British Government. In 1928 he was appointed professor of protobiology at Yale University, from which post he retired in 1933 to found the Laboratoire du Bacteriophage,

Digitized by Google

Paris. Between 1934 and 1936 he set up for the government of the U.S.S.R. bacteriophage research institutes at Tiflis, Kiev, and Kharkov.

His description of the phenomenon of bacteriophage which bears his name was published in 1917, in a note to the French Academy. The phenomenon had been discovered earlier by F. W. Twort (1915), but the graphic account given by d'Herelle, on his independent discovery of it, startled the scientific world. The therapeutic aspects of this work never enjoyed the support and enthusiasm in England that they achieved elsewhere, which must have been a deep disappointment to him.

He received many honours, of which he especially prized the Leeuwenhoek medal of the Amsterdam Academy of Science (1925), and the M.D. Leyden (1923)—the former because the only previous French scientist to receive the distinction was the great Louis Pasteur (1895), and the latter because among the very few British recipients of a doctorate of the University of Leyden was Winston Churchill (1946).

A clear thinker, with an impeccable laboratory technique, and endowed in high degree with the logical outlook of his race, d'Herelle appeared at times somewhat intolerant to those who differed from him; yet to his friends and associates he was one of the kindest and most loyal of men. He leaves two daughters and three grandchildren.

Appointments

DICK, A. P., B.A., M.D. Camb., M.R.C.P.: visiting physician, East Ham Memorial Hospital.
HIGHAM, A. R. C., M.B. Lond., F.R.C.S.: visiting genito-urinary surgeon, Queen Mary's Hospital for the East End, London.
KEITH, GLADYS, M.B. Lond., F.R.C.S., M.R.C.O.G.: obstetrician and gynæcologist, Oldchurch Hospital, Romford.
LAW, W. A., O.B.E., M.A., M.D. Camb., F.R.C.S.: visiting orthopædic surgeon, Seamen's Hospital, Tilbury.
SALMON, H. W., M.D. Lond., M.R.C.P.: visiting physician, East Ham Memorial Hospital.
STEWART, E. F. G., F.R.C.S.: visiting ear, nose, and throat surgeon, Hackney Hospital.
STURTON, R. V., M.R.C.S., D.A.: visiting anæsthetist, Stratford and Forest Street Clinics, London.
WATT, J. D., M.B. Edin., M.R.C.O.G.: obstetrician and gynæcologist, Oldchurch Hospital, Romford.
WILSON, HELEN, M.B. Durh.: medical inspector of European schools in Northern Rhodesia.

The Hospital for Sick Children, Great Ormond Street, London:

D'ARCY, JOAN, M.B. Belf., asst. resident M.O., Tadworth Court.
DUNN, H. G., M.A., M.B. Camb., M.R.C.P.: house-physician.
FISHER, O. D., M.B., M.R.C.P., D.C.H.: house-physician.
JOHN, BEATRICE, M.B. Aberd.: house-surgeon.

Births, Marriages, and Deaths

BIRTHS

DAVIS.—On April 6, in London, to Dr. Renate Davis (née Loeser), wife of Mr. Albert Davis, F.R.C.S.—a son.
MACLEOD.—On April 7, in London, the wife of Dr. W. M. Macleod—a daughter.
O'SULLIVAN.—On April 11, the wife of Dr. J. G. O'Sullivan—a daughter.
POTTER.—On April 8, in London, the wife of Dr. J. M. Potter—a son.
SCOTT.—On April 7, at St. Albans, the wife of Dr. T. A. L. Scott—a son.
TAYLOR.—On April 11, in Edinburgh, to Dr. Helena Taylor (née Lauder Thomson), wife of Dr. A. W. O. Taylor—a son.
VICKERS.—On April 12, at Sheffield, the wife of Dr. H. R. Vickers—a daughter.
WHEELER.—On April 7, at Aylesbury, the wife of Surgeon-Commander S. J. Wheeler, R.N.—a son.

MARRIAGES

HOLGATE—BRIERLY.—On April 5, at Upper Hopton, John Aitken Holgate, M.B., to Carol Brierly.
WHEELER—WEARE.—On April 5, at Rainham, Kent, Richard Handley Wheeler, M.B., to Sheila Kathleen Weare.

DEATHS

CUTHBERT.—On April 7, in Glasgow, Charles Campbell Cuthbert, M.A., M.D. Glasg.
DAVIES.—On April 6, John Christopher Davies, B.A., B.M. Oxfd.
D'ESTERRE.—On April 12, in London, William Henry Daniel Patrick d'Esterre, M.D. Durh., aged 79.
MCKIE.—On April 6, at Eastbourne, Gordon McKenzie McKie, M.R.C.S., aged 76.
NEILL.—On April 9, at Coonoor, South India, the Rev. Charles Neill, M.A., M.B. Camb., aged 80.
SORSBY.—On April 6, at Los Angeles, Maurice Sorsby, M.D. Leeds., F.R.C.S.E.
WACHER.—On April 11, Harold Wacher, B.A., M.D. Camb.
WILLANS.—On April 6, at New Milton, Hants, Charles Rudolph Willans, M.B. Manc.

Notes and News

REGIONAL ORGANISATION OF MINISTRY OF HEALTH

SINCE 1945 the Minister of Health has had principal housing officers in each region. Their functions have now been transferred to principal regional officers, who will also undertake the duties previously performed by general inspectors and the regional officers for health services, whose appointments as such will be brought to an end. The principal regional officers will have no executive functions in relation to regional hospital boards, hospital management committees, boards of governors of teaching hospitals, executive councils, and local health authorities; but, in collaboration with the principal medical officers for the regions, they will maintain close contact with these bodies so as to exchange information and keep the Minister informed of local developments.

The principal medical officers work on the basis of hospital regions and operate mainly from Whitehall. Broadly, the arrangement is that a principal medical officer deals with a group of three regional hospital boards and with the local health authorities and local authorities wholly or mainly within those hospital regions. Each principal medical officer has a small team of medical and nursing officers working under him, and in some instances one of these medical officers is stationed at the Ministry's regional office. The names of the principal medical officers and their medical staff are:

Newcastle, Leeds, and Sheffield Hospital Regions

Dr. G. Lilico. Medical officers: Major-Gen. A. D. Fraser (at Newcastle), Dr. K. M. Hirst, Dr. Johnstone Jervis (at Leeds), Major-Gen. R. W. D. Leslie (at Nottingham), and Dr. D. M. Lyon.

East Anglian, N.W. Metropolitan and N.E. Metropolitan

Dr. A. L. Banks. Medical officers: Dr. R. M. Shaw, Dr. C. Sims-Roberts, and Dr. D. S. Todd-White.

S.E. Metropolitan, S.W. Metropolitan, and Oxford

Dr. G. E. Godber. Medical officers: Dr. M. Manson, Dr. A. E. Martin, and Dr. A. L. Winner.

South-Western

Dr. J. Ferguson. Medical officers: Dr. R. Elliott and Dr. C. Grant Nicol.

Manchester and Liverpool

Sir Alexander Hood. Medical officers: Dr. M. G. Gorrie and Dr. J. M. Ross (at Manchester).

Birmingham

Dr. G. A. Clark. Medical officer: Dr. C. A. Seeley (at Birmingham).

THREE IN A LINE

IN *The Three Churchills* [1] Sir Arthur MacNalty has written short biographies of "Corporal John," Lord Randolph, and Mr. Winston Churchill. It is a work of frank piety, to honour three great men, and contains little new but all refreshed. Do such families transmit other legacies to their offspring than a famous surname? Traditional exogamy has given English society a flexibility which has assured its persistence; marriage within sixteen quarterings has reduced other aristocracies to impotent decadence. Again and again Spanish gene has linked with Spanish gene, and a wearer of the Golden Fleece today might be from the brush of Velasquez. In England fancy and financial advantage have united peer and commoner for a thousand years, and it is no more than wishful romanticism that sees a Stuart upper lip on this or that noble lord of royal (though left-handed) ancestry diluted with an infinite variety of genes at each generation. So it is that in each of these Churchills we may perhaps find a gift of achievement grounded in application, a political prescience above their contemporaries' (but Lord Randolph "forgot Goschen"), a certain contempt for mere consistency. But there is no Churchill facies; and no-one would dare to claim that mental characters such as these are enough to identify the family. It is wise to remember too that, once the dukedom had reached the Spencer line, it was a hundred and fifty years before a member of the family earned more than a few words in the encyclopædia.

Where is Bohun? where Cromwell? where Wellesley or Wesley? The names are in the telephone directory, but it is no ordinary blow which strikes a chip off the old block. Surely it is not the genes of John and Sarah but some lucky coincidence of the stars which we must thank for the voice and the man who saved us in 1940.

1. The Three Churchills. London: Essential Books. 1949. Pp. 268. 10s. 6d.

Digitized by Google

TOXICITY OF NEW INSECTICIDES

THE risks from some of the new insecticides, which we discussed in a leading article last week, have lately been underlined by Dr. James Wilson, secretary of the American Medical Association's council on pharmacy. At a meeting of the American Chemical Society in San Francisco, Dr. Wilson complained, says B.U.P., that some manufacturers had placed powerful insecticides on the market before compiling full information about their toxicity; and he suggested that the public should be protected against these substances as against dangerous drugs.

MATERNITY BENEFIT

UNDER the National Insurance (Claims and Payments) Provisional Amendment Regulations, 1949, which came into force on April 14, mothers are allowed more time in which to claim maternity benefits. The maternity grant of £4 can now be claimed at any time from 11 weeks before the expected week of confinement up to 3 months after the confinement. The attendance allowance of £1 a week for 4 weeks after confinement can now be claimed at any time between the 11th week before the expected date of confinement and the 4th week afterwards. The maternity allowance, a special benefit in place of attendance allowance for mothers who usually work for employers or in their own business, can be claimed between the 11th and 6th week before the expected confinement. The certificate of expected confinement can now be completed by the doctor at any time between the 11th and 6th week before confinement. The time for notifying the date of confinement has been extended from 3 to 4 weeks after confinement.

LINCTUS DIAMORPHINÆ

THE *National (War) Formulary* ceases to be operative from May 1, and since there is no linctus diamorphinæ in the new *National Formulary*, pharmacists will be unable, under the Dangerous Drug Regulations, to dispense the *N.(W.)F.* preparation unless the formula is written out in full. In order to overcome this difficulty, the Pharmaceutical Society has released its formulæ for the two linctuses which are scheduled for inclusion in the *B.P.C.*, 1949, which has not yet been published; their composition was recorded in the *Pharmaceutical Journal* of March 26. This gives two *B.P.C.* linctuses—linctus diamorphinæ *B.P.C.* (the same strength as the *N.(W.)F.* linctus but with a different base), and linctus diamorphinæ et hyoscyami *B.P.C.* When, therefore, after May 1, a doctor prescribes linctus diamorphinæ or linctus diamorphinæ *N.(W.)F.*, pharmacists will dispense linctus diamorphinæ *B.P.C.* unless a formula is written out in full.

AN APPOINTMENT TERMINATED

AN unusual situation was considered by the North-West Metropolitan Regional Hospital Board at its meeting on April 11. The board's establishment committee reported that the name of Dr. R. McGowan, who held an interim contract with the board as pathologist at Uxbridge Cottage Hospital and Uxbridge Isolation Hospital, was not on the British Medical Register. The contract has been terminated. The *Daily Mail* (April 12) reports Dr. McGowan as saying that he qualified twenty years ago at Harvard University.

POISONS RULES AND LIST

THE Poisons Rules, 1949 (Statutory Instrument no. 539) supersede the original Rules and the amending Rules which have since been made from time to time; and they include a number of changes announced earlier this year (see *Lancet*, Jan. 15, p. 129, and Feb. 12, p. 289). The Poisons List has been brought up to date by the Poisons Order, 1949 (Statutory Instrument no. 538).

University of Oxford

The George Herbert Hunt travelling scholarship for 1949 has been awarded to Dr. D. R. Wood, of Brasenose College.

National University of Ireland

On April 7 the following degrees were conferred:

M.D.—J. K. Feeney, J. W. Harman.
Ph.D.—Fergus O'Rourke.

Dr. William Kearney was appointed to the professorship of obstetrics and gynæcology at University College, Cork, and Dr. John McGrath to a part-time lectureship in pathology and bacteriology at University College, Dublin.

University of London

Dr. N. H. Martin has been appointed to the readership in chemical pathology at St. George's Hospital medical school as from April 1.

Dr. Martin graduated with honours in chemistry at the University of Durham in 1928 and as Phillip Buckle travelling fellow went to Munich and Berlin to continue his postgraduate studies. In 1929 he returned to London and, after a further year of research in chemistry, was awarded the diploma of the Imperial College and became a fellow of the Royal Institute of Chemistry in 1930. In 1931 he went to Oxford to study medicine, taking the honours course there under Professors Sherrington and Peters. Continuing his medical studies at the Middlesex Hospital, where he was a demonstrator in the Courtauld Institute, he qualified in medicine in 1936 and held house-appointments in the hospital. He was appointed assistant pathologist in the Bland-Sutton Institute in 1939. During the late war he served in France and Africa, being appointed assistant director of pathology to the 21st Army Group and the British Army of the Rhine. He was twice mentioned in despatches for his services in the war. On release he returned to the Bland-Sutton Institute, but was released to UNRRA as deputy consultant in nutrition to the European Zone. Appointed to a Rockefeller fellowship in 1945 he studied at Harvard Medical School under Professors Janeway and Cohn. In 1946 he was appointed a research fellow in Harvard University and assistant in medicine to the Peter Bent Brigham Hospital. He returned to England in 1947 to take charge of the chemical pathology laboratories at St. George's Hospital. He has published papers on infective hepatitis, serum hepatitis, and protein distribution and disturbance in disease states.

Mr. A. J. Marshall, D.PHIL., has been appointed to the readership in zoology and comparative anatomy at St. Bartholomew's Hospital medical college as from Oct. 1.

On Monday, April 25, at the London School of Hygiene, Keppel Street, W.C.1, Dr. A. Gratia, professor of parasitology and bacteriology in the University of Liége, will speak on Bacteriophage and Antibiosis. Prof. Kl. Gollwitzer-Meier (Hamburg) is to give three lectures at King's College, Strand, W.C.2. On May 13 he is to speak on Heart Metabolism and Coronary Disease, on May 16 on Venous Return in Health and Disease, and on May 18 on Blood-reaction and Blood-flow in Muscular Activity. Mr. Rudolf Brdička, associate professor of physical chemistry in the Charles University, Prague, on May 24 and 26 at the Westminster Medical School, Horseferry Road, S.W.1, will discuss Applications of Polarography to Medicine. All these lectures will begin at 5.30 P.M.

University of Leeds

Prof. G. Grey Turner will give the Moynihan lecture in the Riley-Smith Hall of the University Union on Monday, April 25, at 3 P.M. His subject is to be Moynihan and the Training for Surgery.

Royal College of Obstetricians and Gynæcologists

The diploma in obstetrics of the college has been conferred on the following:

Philip Allebone, Margaret Bagshaw, Umes Chandra Bardolai, E. L. Barr, Aileen V Barrett, W. A. Benson, Kathleen N. Berger, S. W. Beswick, G. F. Bigwood, P. M. Brett, D. M. Brodie, Margaret Brodigan, G. H. Burgess, Elizabeth B. Butler, Rachel Cameron, Kevin G. Casey, Jean Cleghorn, W. W. Coppinger, A. C. Coulthard, J. K. Craig, Samuel Dalziel, J. A. R. Debenham, Dhireshwar Shankardas Desai, Gerald Dison, Janet McK. Donald, Freyda F. Dougall, R. W. Drewer, Mary E. Egan, T. H. Eustace, Marjory F. Foyle, R. L. Gadd, J. E. Gilbert, Philippa A. Glyn, Beryl J. Goff, Leonard Goodman, G. E. L. Graham, E. P. Griffiths, Wilhelm Gross, Harry Hanson, J. G. Harrison, A. P. B. Harston, Vivien P. Helme, M. J. T. Hewetson, Mary Higgs, Agnes M. Highet, T. R. Hunt, Rachel Jacobs, S. T. James, C. M. Jones, Nest M. Jones, D. H. Joseph, Sanmugam Kanapathippillai, C. H. Kaye, Katie Keane, Katherine M. Kelly, H. A. Kent, R. F. Kingston, A. I. I. Klopper, H. J. Knight, G. W. Korn, G. D. Lees, Lillian J. Letty, J. C. S. Leverton, M. G. H. Lewis, G. H. Lloyd, H. J. Love, Jessie B. Macaulay, Angus MacLellan, R. L. Macpherson, Declan Magner, Achy Mathew, Mary I. Milne, Mohini Mirchandani, Catherine H. Mitchell, L. O. Morgan, Monica M. A. Murphy, Barbara J. Nathan, L. M. Norburn, Susan B. G. Ofori-Atta, Hugh O'Hara, N. L. Owen, Ethel W. W. Owston, Teng-Cheung Pang, W. M. Patterson, Pauline M. Philpott, G. D. Pinker, Jessie M. Pope, Brian Pownall, D. B. Price, Delmont Puflett, Eby Quehl, Mairead M. Robinson, Oswald Rosensweig, W. I. Russell, Margaret M. P. Ryan, Jean M. Sandel, Eileen P. Scanlan, R. D. Simpson, J. M. Slattery, F. G. M. Smith, J. S. Smith, Roberta A. Stewart, R. J. Still, Kollengode Subramani Subbalakshmi, H. P. Tarnesby, J. S. Taylor, Alice P. Thomas, Glenys M. Thomas, T. A. Thompson, H. S. Trafford, Doreen G. Warnock, J. L. Warren, P. F. A. Watkins, N. E. Wood.

Royal Medico-Psychological Association

A meeting of the child psychiatry section of this association will be held at 1, Wimpole Street, London, W.1, on Saturday, April 23. At 11.15 A.M. Dr. Mildred Creak and Dr. R. H. Dobbs will speak on the Psychiatric Aspects of Maternity and Child-Welfare Work, and at 2.15 P.M. Miss Anna Freud and Dr. A. G. Watkins on the Effects of Hospitalisation on the Child.

Digitized by Google

Society of Apothecaries of London

A further course of ten lectures on modern therapeutics will be held by the society in the week beginning Dec. 5.

Central Midwives Board

Mr. Arnold Walker has been re-elected chairman, and Mr. J. P. Hedley vice-chairman, of the board for the coming year.

Scottish Health Advisory Committees

The chairmen of these committees (*Lancet*, Feb. 19, p. 320) include the following: Sir Sydney Smith (medical advisory committee), Dr. R. C. Scott Dow (dental advisory committee), Dr. A. F. Wilkie Millar (advisory committee on health centres).

London County Medical Society

A clinical meeting will be held at 4 P.M. on Wednesday, May 4, at Bethnal Green Hospital in conjunction with St. Leonard's Hospital. Further information may be had from the hon. secretary, Mr. J. Gabe, St. Alfege's Hospital, Vanbrugh Hill, S.E.10.

West London Medico-Chirurgical Society

The annual banquet of this society will be held on Wednesday, May 18, at the Royal College of Surgeons, Lincoln's Inn Fields, W.C.2, at 8 P.M., when Lord Moran will present the triennial gold medal to Prof. R. A. McCance, F.R.S.

West London Hospital

Mr. R. C. Brock will deliver the second Alex Simpson Smith lecture at 11, Chandos Street, London, W.1, on Wednesday, June 15, at 8.30 P.M. He is to speak on the Surgical Treatment of Congenital Pulmonary Stenosis. Lieut.-General Neil Cantlie, director-general of Army Medical Services, will be in the chair. Tickets may be had from the dean of the medical school, West London Hospital, W.6.

Central Council for the Care of Cripples

On Friday, April 29, this Council will hold a conference at the Conway Hall, Red Lion Square, London, W.C.1, at 10.30 A.M. on Planning the Future for the Physically Handicapped. Speakers will include Mr. H. Osmond-Clarke and Dr. G. S. Wigley. Further information may be had from the secretary of the council, 34, Eccleston Square, S.W.1.

Hospital Endowments in Scotland

The Secretary of State for Scotland has announced that the first meeting of the Hospital Endowments Commission will probably be held shortly after Easter. The commission is a purely Scottish body, and there is no corresponding body under the National Health Service in England and Wales. The members include Sir Sydney Smith (chairman) and Dr. A. Greig Anderson.

General Medical and Pharmaceutical Services

The National Health Service (General Medical and Pharmaceutical Services) Amendment Regulations, 1949, include an amended and extended list of appliances which may be prescribed on form E.C.10 by a general practitioner and dispensed by a chemist. A new regulation empowers executive councils as an exception to permit a practitioner providing maternity medical services to employ a deputy or assistant whose obstetric experience has not been approved by the local obstetric committee.

Tuberculosis Conference

The second Commonwealth and Empire Health and Tuberculosis Conference is to be held in the Central Hall, Westminster, London, from July 5 to 8. Representatives from 17 Dominions and Colonies are expected and visitors from 16 other countries. Mr. Arthur Creech Jones, Secretary of State for the Colonies, is to speak on the Organisation of Comprehensive Tuberculosis Schemes in a British Colony, and Dr. Edith Summerskill, parliamentary secretary to the Ministry of Food, on Protection from Bovine Tuberculous Infection. There will also be discussions on modern treatment for tuberculosis, including streptomycin and P.A.S.; the policy of B.C.G. administration; and psychological and social readaptation of chronic disease in industry. The speakers will include: Dr. P. V. Benjamin (India), Dr. W. E. Chiesman, Dr. J. Greenwood Wilson, Prof. Jorgen Lehmann (Gothenburg), Dr. T. A. Lloyd Davies, Dr. John Lundquist (Stockholm), Dr. J. B. McDougall (W.H.O.), Dr. R. B. Macgregor (Malaya), Dr. Geoffrey Marshall, Dr. J. E. Perkins (U.S.A.), Mr. C. Price Thomas, Dr. Charles Wilcocks, Dr. A. B. Williamson. Further information may be had from the N.A.P.T. Tavistock House North, London, W.C.1.

Victor Horsley Memorial Fund

Sir Hugh Cairns has been appointed Victor Horsley lecturer for 1949.

Society of Chemical Industry

On Wednesday, May 18, at 6.15 P.M., at the London School of Hygiene, Keppel Street, W.C.1, the nutrition panel of this society will hold the second of its series of meetings on manufactured foods, when the subject for discussion will be Biscuits, Cakes, and other Flour Confectionery.

Dr. Frederick Himmelweit has been appointed a chevalier of the Order of the White Lion by the president of the Czechoslovak republic.

CORRIGENDA: *The General Practitioner*.—The author of the second letter under this heading last week (p. 669) was Dr. C. A. H. Watts. In Dr. Ballance's letter under the same title, the 18th line of the third paragraph should read "increased precision in the indications for surgery in peptic ulcer."

Diary of the Week

APRIL 24 TO 30

Monday, 25th

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS, 58, Queen Anne Street, W.1
NOON. Dr. V. Mary Crosse: Prematurity.
5 P.M. Mr. R. Christie Brown: The Infertile Marriage.

UNIVERSITY OF LONDON
4.45 P.M. (University College, Gower Street, W.C.1.) Prof. Adrien Albert: Selective Toxicity with special reference to Chemotherapy. (First of eight lectures.)
5.30 P.M. (London School of Hygiene.) Prof. A. Gratia (Liége): Bacteriophage and Antibiosis.

WESTMINSTER MEDICAL SCHOOL, Horseferry Road, S.W.1
5.30 P.M. (Meyerstein lecture theatre.) Clinico-pathological meeting on Cerebral Aneurysms.

HUNTERIAN SOCIETY
7.30 P.M. (Talbot Restaurant, 64, London Wall, E.C.2.) Mr. H. St. John Rumsey: Speech Defects and Voice Affections.

Tuesday, 26th

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Prof. G. I. Strachan: Non-malignant Conditions of the Cervix.
5 P.M. Dr. A. Melvin Ramsay: Modern Trends in Puerperal Infection.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
2.30 P.M. Mr. W. A. Mill: Malignant Diseases and Radiotherapy.

Wednesday, 27th

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Miss Alice Bloomfield: General Surgical Conditions in Gynæcological Practice.
5 P.M. Mr. R. A. Brews: Endometriosis.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Mr. Joseph Minton: Occupational Eye Diseases and Injuries. (Second lecture.)

Thursday, 28th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Prof. C. F. M. Saint: Stomatodæal Ruminations. (Hunterian lecture.)

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Mr. Percy Malpas: Radiotherapy in Non-malignant Gynæcological Diseases.
5 P.M. Prof. W. I. C. Morris: The Contracted Outlet.

FACULTY OF RADIOLOGISTS
8.15 P.M. (32, Welbeck Street, W.1.) Dr. F. Gordon Spear: Sylvanus Thompson lecture.

MEDICO-LEGAL SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Surgeon Lieut.-Commander John Bunyan, L.D.S., Mr. C. W. Stidson Broadbent: Medicolegal Aspects of Problems of Everyday Dental Practice.

HONYMAN GILLESPIE LECTURE
5 P.M. (Anatomy theatre, University New Buildings, Teviot Place, Edinburgh.) Prof. T. Ferguson: A Workshop for Severely Disabled Men.

Friday, 29th

ROYAL COLLEGE OF SURGEONS
5 P.M. Prof. R. I. Harris (Toronto): Spondylolisthesis. (Hunterian lecture.)

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS
NOON. Miss Isobel Beswick: Metropathia Hæmorrhagica.
5 P.M. Mr. J. V. O'Sullivan: Third Stage of Labour.

FACULTY OF RADIOLOGISTS
2.15 P.M. (Royal College of Surgeons.) *Therapy Section and R.S.M. section of radiology.* Prof. B. W. Windeyer, Dr. J. S. Fulton, Dr. Percy Stocks: Presentation of Results in the Treatment of Cancer.
8.15 P.M. (1, Wimpole Street, W.1.) Dr. Ralston Paterson, Miss M. C. Tod, Prof. R. McWhirter will continue the discussion.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASE, 11, Chandos Street, W.1
8 P.M. Dr. A. H. Harkness: Reiter's Disease.

Digitized by Google

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

CHRONIC BRONCHITIS

NEVER A COMPLETE DIAGNOSIS *

W. A. LISTER
T.D., M.A., M.D. Camb., F.R.C.P.
PHYSICIAN TO THE SOUTH DEVON AND EAST CORNWALL HOSPITAL, PLYMOUTH

CHRONIC bronchitis is one of the commonest diagnoses, and because it is traditional it is accepted without question and regarded as final and satisfactory. Yet, if one consults the textbooks on this subject one finds little precision; the classifications given seem to be confused, unscientific, and unhelpful in deciding on a rational course of investigation and treatment.

Broadly speaking, the clinical picture so often described as chronic bronchitis comprises cough, shortness of breath, and the production of sputum. The condition may be more or less continuous, or there may be attacks tending to become more frequent over the months or years.

In my experience the great majority of patients showing this syndrome are in fact sufferers from a mild degree of asthma; but before discussing this proposition in detail I shall say a few words about other somewhat less common, but extremely important, conditions which are often wrongly diagnosed as chronic bronchitis because this diagnosis is so readily accepted that it does not come under proper scrutiny.

MISDIAGNOSES

One of the states widely misdiagnosed as chronic bronchitis is a mild degree of *left-ventricular failure.* Elderly people who are the subjects of arteriosclerosis, with or without hypertension, often carry on, despite a certain amount of breathlessness on effort, until an infective illness tips the scale against them, either by toxic action on the ventricular muscle or by inducing auricular fibrillation. The state of the heart should always come under suspicion in such a patient if a "feverish cold" or attack of influenza fails to clear up in a week or two under appropriate treatment, and if cough, sputum, and breathlessness continue. Crepitations will persist more or less symmetrically at the lung bases. In the heart itself the suggestive signs are tachycardia with "gallop rhythm" if the pulse is regular, or a totally disorderly rhythm indicating auricular fibrillation, even though the rate may not be unduly raised. The heart may be, and often is obviously enlarged, and the blood-pressure raised. Expectorants will be useless in such circumstances, and three or four weeks of complete bed rest with digitalis or mersalyl are indicated.

Secondly, "Chronic Suppurative Bronchitis" is described as an entity in the latest edition of Price's *Medicine,* when cough is accompanied by copious purulent sputum. No suggestion is made that a *focus of sepsis in the upper respiratory tract* may be the cause. It is my conviction that purulent sputum does not persist in the absence of some primary disease or focus of infection in the respiratory tract. An infected antrum is the commonest cause. It is often overlooked, and even X-ray films of the antra cannot be relied on to establish the diagnosis. The patient may give no hint of any local symptoms in his history; but a deflected septum, pus in the naso-pharynx, nasal obstruction, or evidence of otitis media should rouse one's suspicions and indicate a check by an ear, nose, and throat specialist.

I remember seeing some years ago a strapping young officer in the Royal Merchant Navy, who, in addition to a chronic cough and copious purulent sputum, had extensive peripheral neuritis and paroxysmal auricular fibrillation. He was discharged from the service as incurable, and was in a deplorable bedridden state. Both his antra were full of pus, and when these were drained he made a rapid and complete recovery and eventually re-entered the service and served throughout the war.

Such a vivid experience impressed on me the importance of investigating the sinuses when faced with such a case, and time after time the search has proved successful. Davidson (1949) makes the same point and quotes another dramatic example.

If a focus of infection cannot be found in the nose, the chest should invariably be radiographed, for one may be dealing with some local disease of the lung such as bronchiectasis, cystic disease, abscess, or possibly a cancer. This is not the place to discuss these states in detail. The point I wish to make is that if the sputum is persistently purulent it strongly suggests some primary local disease, either in the nose or in the lung itself, and a search for such a focus should never be omitted.

Chronic *senile phthisis* is another condition which may drag on for years unsuspected, and the patient may come to be regarded as just another chronic bronchitic. The patients and their relatives are often so accustomed to their symptoms, and have had so little help from medicine, that they are averse from again visiting their doctor for a detailed overhaul, and the true state of affairs is only brought to light when some young member of the family develops acute tuberculosis, possibly meningitis, and all contacts are reviewed. Then, of course, it is too late, and the damage is done; for the sputum of the supposed chronic bronchitic is found to be loaded with tubercle bacilli. Diagnosis on clinical grounds may be far from easy unless the sputum is tested, because local signs are overlaid by those of emphysema and generalised bronchial catarrh.

Bronchitis due to direct *irritation* is also mentioned in "Price." Irritation from tobacco smoke is by far the commonest, and in my view the only legitimate, member of this group. It is perhaps less often seen in these days of austerity. Chronic alcoholics often oversmoke. Silicosis is a disease by itself and the patient's occupation should arouse suspicion. Byssinosis in cotton workers and "farmer's lung" are in my view allergic states due to the inhalation of moulds. They should be classified as asthma. Pensioners from the 1914–18 war regarded as suffering from the effects of gas are now at any rate to be regarded as asthmatics, though no doubt in many of them damage caused by the gas determined or aggravated their essential allergic tendency.

BRONCHOSPASM

In all the conditions so far touched on, some degree of bronchospasm may occur and may mask the primary state. Cardiac asthma is an obvious instance. All that follows is written on the assumption that this is appreciated and any primary disease has been excluded. I shall not discuss classical asthma, with clear-cut paroxysmal attacks: the diagnosis here is obvious.

Having now cleared the ground, we are left with a mass of clinical material commonly diagnosed as chronic bronchitis. Considering its importance, it is surprising how little attention is paid to it in our teaching hospitals. I cannot recall ever having a house-physician who had received instruction on it. In the textbooks it is described under various sub-headings and types, little related to any logical system of pathology and treatment. The accounts given under the headings "catarrhal" and "fibrinous" bronchitis in the latest edition of Price's *Medicine* are examples. And here is an extract from a paper by Southwell (1946) on the use of penicillin inhalation in the asthma clinic at Guy's Hospital? He is describing his classification of the patients treated:

The *bronchitic* patients could be subdivided into two groups: those with symptoms of short duration, and the chronic cases. The former comprised 6 patients, of whom

* Based on an address to the West Country Physicians Club.

Digitized by Google

5 were known to be "bronchial" and had bronchitis, which had followed a recent head cold. All had much cough and some thick tenacious sputum and were wheezy at night.

The second group, or chronic bronchitics, could be further subdivided into suppurative and non-suppurative cases; the latter were typical examples of chronic bronchitis and emphysema. The patients had many years' history, and all had severe symptoms, both in winter and in summer. There were associated bronchospasm and shortness of breath in all these cases but no attacks of paroxysmal dyspnœa.

The *asthmatic* patients were all established cases, and were chosen, except 4 allergic cases, not only because they were comparatively static and therefore allowing of more reasonable assessment, but also because they were considered to be examples of bronchitic asthma in which the allergic element was minimal, and the underlying condition one of recurrent or chronic bronchial mucosal infection. On the whole, their major asthmatic attacks were fairly evenly spaced but were not such a prominent feature of their illness as was the case in the small allergic group.

Coming from such a source, this indicates the present view in our teaching schools, and it illustrates my point precisely. Surely all these patients are essentially asthmatic? The only variables are the degree of secondary infection and the rhythm and severity of the bronchial spasm.

I wish to make the following points:

1. That asthma—i.e., an allergic bronchial spasm—is the essential element of all this group.
2. That generalised emphysema is an end-result and a hallmark of an underlying asthmatic state.
3. That infection may occasionally be a primary cause, but is far more commonly secondary.

THE ALLERGIC BASIS

Chronic asthma commonly makes its first appearance in childhood. Vasomotor rhinitis—which after all is merely an allergic reaction in another part of the respiratory tract—is a closely associated accompaniment. We all know only too well the child who is "always catching cold" or who is regarded as "bronchial," to quote Southwell again. These "colds" are "head colds" with nasal catarrh and a watery secretion initially. The mother will describe how after a few days the cold flies to, or settles on, the chest, and for a week or more there is cough, thick sputum, and wheezing at night. The child usually cannot run and play games as well as other children, owing to shortness of breath. There may be some degree of fever with the attacks. On examination the children are generally found to be mouth-breathers, with high arched palates, and they are prone to secondary infective states such as otitis media.

As age advances towards adolescence the attacks become less conspicuous, and in the prime of life they may cause comparatively little disability, though extra stress such as hard military training in war-time or service in a foreign climate may aggravate them and a pension may be awarded. In later life they conform precisely to Southwell's "chronic bronchitics."

Minor degrees are common. A typical example is the elderly or middle-aged patient with a hernia, whose surgeon wishes to operate but finds him to be "a bit chesty" and so asks for a second opinion. We find a patient with a rigid chest, a cough, and expiratory ronchi which are made more conspicuous by coughing or forced expiration. Careful inquiry will frequently elicit a past history such as I have indicated, and the existence of allergic symptoms in other members of the family.

EMPHYSEMA

This brings me to my second point, that generalised emphysema is an end-result and hallmark of a chronic asthmatic state. The bulky lungs found post mortem are not now our concern, except that I suggest that this condition might reasonably be expected if the lungs have been over-inflated for most of a lifetime. The clinical features are well known—the deep chest, rounded back, hunched shoulders, wide costal angle, and limited range of expansion. Radiographically the appearances are equally characteristic, though it is surprising how seldom they are commented on by radiologists. The ribs spring upwards from their attachment to the vertebræ, giving the impression of a toast-rack. The intercostal spaces are unnaturally wide and the whole chest has an oblong, box-like shape. The diaphragm is flattened and the costophrenic angles are unusually wide. The shadows of the pulmonary vessels and bronchi at the hila show conspicuously in contrast to the translucent lung fields. The clavicles are often unnaturally elevated. Films are usually taken when the patient has been asked to draw a breath; so vigorous coöperation on the part of a healthy subject may in some instances and in some degree produce these appearances. After all, they merely show that the limit of forced inspiration has been reached. But healthy subjects seldom expand their chests to this extent even at the request of a radiologist, whereas asthmatics habitually do so. As always, the chest film must be correlated to the clinical picture. It is a commonplace that bronchial spasm, by inhibiting expiration, leads to a state of over-inflation. I suggest that the converse is true—namely, that a fixed state of over-inflation is proof of prolonged bronchial spasm, or (if you prefer it) asthma.

INFECTION

My last point concerns the relationship of microbic infection to asthma. A comparison with eczema or "dermatitis," another allergic disease often associated with asthma, may be helpful. By no means all examples of eczema—indeed, rather a minority—take an acute and dramatic form such as one sees when a sensitive individual is exposed to primula plants or to certain hair-dyes. Far more often eczema is subacute or chronic, and tends to affect those in late or early life, and the allergen responsible is anything but obvious. These two extremes have their precise counterpart in asthma.

Further, eczema is seldom if ever caused by pyogenic bacteria, though often by moulds and allied organisms, such as an epidermophyton or the pityrosporon of Malassez. Secondary infection by pyogenic organisms of an eczematous area is, however, a commonplace. Similarly moulds are frequently the cause of asthma. Farmer's lung and byssinosis have already been mentioned as examples. Pushing the analogy to the limit, I would strongly suggest that pyogenic organisms do not cause asthma, and that when they are found in association with asthma they are secondary invaders, precisely as the staphylococci or streptococci are secondary invaders in a case of impetiginised eczema. The congested and unhealthy nasal mucosa of vasomotor rhinitis, often with polypi and obstructed outlets from nasal sinuses, form an ideal site in which secondary infection may become fairly established. Thence they spread easily to the unhealthy mucosa of trachea and bronchi when asthma is present as well. No competent dermatologist would be content with a diagnosis of chronic dermatitis. Neither should we be satisfied with one of chronic bronchitis.

To complete the parallel, lichenification and emphysema can be regarded as the end-results of eczema and asthma respectively, provided they have continued long enough.

MORAL

My thesis is by no means an academic one. It indicates a logical sequence of investigation and treatment which should be followed by us all and which we should impress on our students. They must be taught to distrust chronic bronchitis as a complete diagnosis as they would one of chronic dermatitis or chronic colitis.

Digitized by Google

When confronted with a patient to whom it might seem to apply, the first thing to do is to exclude those diseases briefly mentioned in the first part of this paper. If they are absent, the probability is that you are dealing with a mild case of asthma in which classical paroxysms of dyspnœa are not a feature. Even in the absence of expiratory rhonchi, a history of frequent colds in early life, or allergy in other members of the family, will be suggestive, while clinical and radiological evidence of emphysema will be conclusive confirmation. If purulent infection is present, it is to be regarded as secondary, and an attempt should be made to deal with it by means of antibiotics and the help of a surgeon. Hunt the elusive allergen if you like, but I fear you will have little luck in these elderly subjects.

Having done all that, I suggest that you put my thesis to a therapeutic test. Treat half your patients with antispasmodics and breathing exercises, if possible under a physiotherapist, on the lines advised by the Asthma Research Council's booklet (1934), and the other half on "Mist. Expect." You will not be left long in doubt.

REFERENCES

Asthma Research Council (1934) Physical Exercises for Asthma. London.
Davidson, M. (1949) *St. Bart's Hosp. J.* 53, 40.
Southwell, N. (1946) *Lancet*, ii, 225.

OBSERVATIONS ON A SERIES OF LABOURS

WITH SPECIAL REFERENCE TO PHYSIOLOGICAL DELIVERY

GRANTLY DICK READ
M.A., M.D. Camb.

THIS series of 516 consecutive labours has been analysed to draw attention to the application of the teaching of physiological or natural childbirth (Read 1933).

Physiological childbirth occurs when the structure and function of each organ taking part in parturition are not impaired by any chemical, emotional, or mechanical anomaly. There is no physiological evidence that childbirth should be painful or that pain can serve any useful purpose in labour. Pain is an emotional anomaly, and the cause of pain in uncomplicated labour is fear. Fear of childbirth is an artefact to which society has justifiably succumbed, for medical science has accepted pain as an essential accompaniment to parturition. It is not unreasonable that women, who for generations have suffered, should expect pain and fear the shibboleth of their maternal desires. Fear causes protective nervous discharges throughout the sympathetic nervous system, whose efferent impulses increase the tone of the muscle tissues they supply. In the uterus this causes resistant tension in the circular muscle-fibres of the lower uterine segment. Resistance to the expulsing muscles produces excessive tension, which is recorded as pain by the uterine nociceptors. On the assumption that the theory of the fear-tension-pain syndrome is correct, the women in this series have received instruction during pregnancy and parturition to remove fear and induce a state of mind which is understanding and serene, and a state of body which is physically fit and muscularly relaxed and controlled.

This teaching has been adopted, after trial against controls, in several universities, hospitals (Sawyer 1946), and maternity centres in other countries and, I understand, in the British Isles. Its applicability to hospital practice has been satisfactorily established abroad. The present cases were attended in the wards and private rooms of the Maternity Hospital, Woking. To some extent they were self-selected for reasons unlikely to give the best statistical results. Many women came because of an exaggerated fear of childbirth, either inherent or engendered by previous labours. Of the 31 primiparæ aged 35 years or more, most had shunned pregnancy because they feared it but after reading of childbirth as a physiological function (Read 1942) decided to become pregnant. The women have been grouped in ages and types which show certain clinical characteristics which, if undifferentiated, might give misleading results. The women were given antenatal instruction in simple physical exercises—relaxation and respiration—and in the elementary phenomena of pregnancy and parturition (Read 1946b). Some attended antenatal classes; others were given printed instructions and questioned from time to time on the progress they had made in their preparation. It was found that with experience and organisation little, if any, extra time was required for each case attending the clinic. These labours were conducted with attention to the emotional as well as the physical changes that take place during normal childbirth (Read 1946a). No series of controls was instituted. This report, then, is not intended to be a statistical record and should not be read as such.

The main principles adopted were to avoid interference, pain, and any horror of childbirth. The fear-tension-pain syndrome (Read 1947) was broken down by education designed to eliminate fear and tension. The safety of the mind and body of the mother and the health of the child was embodied in this objective. Without clinical indication such "scientific aids" as local, sacral, spinal, or general anæsthesia were eschewed. In like manner routine analgesia and the empirical use of sedatives were avoided.

METHODS OF DELIVERY

The 516 cases comprised:
429 physiological deliveries (*83·2%*);
52 forcep deliveries (*10·1%*);
28 cæsarean sections (*5·4%*);
and 7 pairs of twins (*1·3%*).

The deliveries of twins were conducted without untoward incident and are not included in this analysis. There was only 1 breech delivery. All breech presentations were turned by external version between 34 and 38 weeks' pregnancy. On few occasions only did "turned breeches" revert from vertex presentation, and only one, with extended legs and very little liquor, could not be turned. No anæsthetic was necessary or desirable for this manœuvre.

RESULTS

Mortality

There were no maternal deaths. One fœtal death is referred to below. During the period in which this series was observed there were 8 premature stillbirths (at 28 weeks or less), including 1 hydrocephalus, 1 anencephalus, and 1 hydrops fœtalis. These are not included in the analysis.

Duration of Labour

The average time taken by each of the three stages of labour are given in table I. These averages are chiefly of academic interest; but the duration of the first stage seems to be appreciably less than is usually cited. It must be remembered that the onset of labour is often impossible to diagnose. Pre-labour contractions, rhythmical contractions without dilatation, dilatation without any preception of contractions, are all conditions often seen when close observation is made. The duration of labour is much less important than the manner of its conduct. The average duration of the second stage in multiparæ suggests that the attendant should be present at $^4/_5$ dilatation at the latest to be any help to his patient.

Digitized by Google

TABLE II—APPLICATION OF FORCEPS, EPISIOTOMY, AND INJURY TO PERINEUM

Group	No. of cases	Physiological deliveries	Forceps deliveries	Episiotomies	Intact perineum	Lacerated perineum		
						1st deg.	2nd deg.	3rd deg.
Primip. under 20 ..	8	7	1 (12%)	3	4	1	0	0
Primip. 20–24	74	69	5 (7%)	4	43	22	5	0
Multip. 20–24	10	10	0	0	9	1	0	0
Primip. 25–29	107	90	17 (16%)	15	48	34	10	0
Multip. 25–29	64	62	2 (3%)	4	42	18	0	0
Primip. 30–34	63	46	17 (27%)	9	36	16	5	0
Multip. 30–34	69	68	1 (1·5%)	2	47	21	1	0
Primip. 35 or more ..	31	24	7 (22·5%)	10	15	4	2	0
Multip. 35 or more ..	55	53	2 (3·6%)	0	31	21	3	0
All ages	481	429	52 (10·8%)	47	275	138	26	0

Forceps, Episiotomy, and Injury to Perineum

The main facts are given in table II, from which it can be calculated that the unaided (physiological) rate was 89%; the number of forceps deliveries in primiparæ 47 (16%) and in multiparæ 5 (2·5%); these cases are further analysed later. The perineum remained intact in 146 (52%) of the primiparæ and 129 (65%) of the multiparæ.

First-degree tears—i.e., all abrasions leaving raw surface of skin or mucosa, numbered 77 (27%) in primiparæ and 61 (31%) in multiparæ, nearly all of the latter being small openings of old scars. Second-degree tears (rupture of perineal body requiring deep suture) numbered 22 (7·8%) in primiparæ and 4 (2%) in multiparæ. Episiotomies numbered 41 (14%) in primiparæ, most of them being for forceps operation, and 6 (3%) in multiparæ. The number of episiotomies apart from forceps operations was 8 (1·6%) of all deliveries. There were no third-degree tears.

Loss of Blood

The estimates of blood-loss up to half an hour after delivery was made to the nearest ounce and are given in table III. No obvious factor was responsible for the variation in amount lost. The losses of 20 oz. or more were, with 2 exceptions, in natural conscious controlled labours without inertia or precipitation. In more than half (6 cases) the perineum was intact, and no laceration of the cervix uteri was seen on examination.

The small amount of blood-loss, almost entirely placental clot, in 68% of the cases is due to (1) the mother being conscious (unanæsthetised); (2) the mother fondling and sometimes suckling the baby immediately the cord has been severed; (3) no interference with the uterus; and (4) the mother being allowed to expel the placenta when the length of the cord shows it to be in the vagina, and when uterine contractions are re-established, often with desire to push down. The shortest time for the third stage is usually 20 min., but the mother may expel the placenta earlier. In physiological labour the uterus is never pummelled and the placenta never forcibly ousted by the attendant. The woman is encouraged to give one long persistent push during a firm uterine contraction. The natural extrusion of the placenta is practically bloodless if the membranes wrap round it and contain the clot. It is described by women as an extremely pleasing sensation.

In 4 cases blood-transfusion was given without delay. As a precautionary measure all patients, on arrival at the hospital, hand to the sister a card stating their blood-group and Rh factor; this is attached to their notes and placed in the labour ward: Rh-negative mother's blood is examined for antibodies at 36 and 39 weeks, at labour, and a week after. Some Rh-negative women in this series bled more freely than Rh-positive women, but the number is too small to preclude coincidence.

One Rh-negative primipara with antibodies bore a baby which rapidly developed anæmia. It weighed 7 lb. and was transfused at once with 60 ml. of compatible blood. It made a rapid and uninterrupted recovery. The mother had had a blood-transfusion 10 years previously during a severe illness.

The only obstetric shock observed was associated with rapid and severe hæmorrhage post partum.

TABLE I—DURATION OF LABOUR

Parity, age-group, and type of labour	No. of cases	Average duration of labour							
		First stage		Second stage		Third stage	Total		
		hr.	min.	hr.	min.	min.	hr.	min.
Primip. under 20:								
Aided.. ..	1	43	10	2	25	15	45	50
Phys... ..	7	14	9	1	23	26	15	58
Primip. 20–24:								
Aided.. ..	5	11	48	2	52	21	15	1
Phys... ..	69	16	26	1	16	21	18	3
Multip. 20–24:								
Phys... ..	10	8	2	0	27	17	8	46
Primip. 25–29:								
Aided.. ..	17	21	0	2	23	16	23	39
Phys... ..	90	17	21	1	25	19	19	5
Multip. 25–29:								
Aided.. ..	2	11	38	1	48	28	13	54
Phys... ..	62	9	17	0	29	19	10	5
Primip. 30–34:								
Aided.. ..	17	28	37	2	28	21	31	26
Phys... ..	46	14	37	1	25	19	16	21
Multip. 30–34:								
Aided.. ..	1	19	45	0	5	5	19	55
Phys... ..	68	8	25	0	23	16	9	4
Primip. 35 or more:								
Aided.. ..	7	29	30	1	7	15	30	52
Phys... ..	24	16	46	1	52	22	19	0
Multip. 35 or more:								
Aided.. ..	2	7	0	2	18	25	9	43
Phys... ..	53	8	15	0	25	19	8	59
Physiological labours:								
Primiparæ ..	236	16	15	1	25	20	18	0
Multiparæ ..	193	8	41		27	19	9	27
Total of all groups	481*	13	58	1	6	19	15	23

* It will be noted that the totals differ in the several tables: this is because in a few cases the data were too incomplete for inclusion.

SEDATIVES, ANALGESICS, AND ANÆSTHETICS

The administration of sedatives, analgesics, and anæsthetics is analysed in table IV. It will be seen that, apart from the 239 mothers (50%) who had no such drug, 47 had chloral and bromide only and 23 had barbiturates only, these sedatives being given to bring sleep in early labour at night; none of these 309 mothers (64% of the total) needed any pain-relieving measures. Morphine or pethidine, with or without chloral and bromide, was given to 87 mothers (18%) because of distress at the first or the second menace (see below). A self-administered analgesic, with or without a sedative, was taken by 34 mothers, and a few whiffs of chloroform from a drop-bottle on to a mask were given to 3 mothers, either at transition from the first to the second stage of labour or at early crowning of the head—a total of 8%. A general anæsthetic plus sedation was given to 48 mothers (10%) for application of forceps.

Digitized by Google

The most effective sedative is understanding attendance on the woman in labour. For those who have difficulty, about 3/5 dilatation of the cervix is the "time of election" for sedation. Pethidine 100 mg. at that phase often allows a controlled and uninhibited labour to develop.

In primiparæ sleep during the early hours of labour is desirable. Those who begin labour in late evening or in the early hours of the morning, as many do, should receive, as an adjuvant to both mental and physical rest, chloral gr. 20 and bromide gr. 20 so the "natural hours of sleep" should be peaceful, if not actually spent in sleep. The sedative is not given to overcome discomfort but to induce a restful initiation into labour. In this series sedatives given in adequate dose at the right time have not been observed to have any influence on the baby at birth or afterwards.

A knowledgeable exhibition of sedatives in the first stage of labour in most cases obviates the desire or the necessity for analgesics or anæsthetics in the second stage. In this way the risk of interference with the natural processes is minimised. Sedatives should never be withheld if a woman shows signs of uncontrollable fear or physical discomfort in the first stage of labour.

First Emotional Menace.—A labour is made or marred by the care and management of the first emotional menace which occurs when the cervix is about 3/5 dilated.

Second Emotional Menace.—This occurs about the transition from the first to the second stage of labour and may be termed the "pain period of labour," since the ultimate and maximal dilatation of the cervix is referred to the lumbosacral region as backache. An analgesic or a sedative should be given at this time, if a controlled second stage is to be assured. The analgesic may be discarded as soon as the backache goes, which usually happens on full establishment of the expulsive reflex. The patient then drifts into the natural amnesia of the second stage.

Third Emotional Menace.—This is experienced when the advancing head meets the floor of the pelvis. The reaction is one of escapism. Complaints of inability to continue, a feeling of utter exhaustion, or of frustration at the absence of any visible result of her efforts are typical signs. Explanation and encouragement often obviate the necessity of analgesics at this menace.

Fourth Emotional Menace.—This is at the early crowning of the head. The feeling of inevitable splitting is sometimes accompanied by an acute stinging or burning pain. If this is excessive, gas and air should be offered and given if desired until full dilatation, when the vulval margin is naturally anæsthetic. The mask may be removed and the patient witness the birth of her child. All women should be offered gas at this point. Few, however, accept it if the transient nature of the discomfort is explained. It should be remembered that the indications for analgesia vary with the interpretation of stimulus. The pain interpretation of stimulus is intensified by exhaustion of either mind or body. Nourishment should therefore be given in an easily assimilable form—especially glucose drinks. Increasing acetonuria is often observed in women with a low pain threshold. More carbohydrate and fluids, with induced sleep, raise the pain threshold, reduce the acetone, and may obviate the necessity for anæsthesia.

TABLE III—ESTIMATED BLOOD-LOSS UP TO HALF AN HOUR AFTER DELIVERY

Group	No. of cases	Blood-loss (oz.)			
		Up to 6	7–10	11–20	Over 20
Primip. under 20 ..	8	3	4	1	0
Primip. 20–24 ..	73*	43	21	7	2
Multip. 20–24 ..	10	7	0	2	1
Primip. 25–29 ..	107	75	18	12	2
Multip. 25–29 ..	64	44	10	9	1
Primip. 30–34 ..	63	46	11	5	1
Multip. 30–34 ..	69	52	8	8	1
Primip. 35 or more	31	16	5	9	1
Multip. 35 or more	55	41	8	5	1
Total	480	327 (68%)	85 (17%)	58 (12%)	10 (2%)

* Loss not recorded in 1 case.

TABLE IV—ADMINISTRATION OF SEDATIVES, ANALGESICS, AND ANÆSTHETICS

Group	Sedatives					Analgesics		Anæsthetics		No sedatives, analgesics, or anæsthetics	Total
	Chloral and bromide (usual dose gr. 20 of each)	Morphine (usual dose gr. 1/4)	Pethidine (usual dose mg. 100)	Chloral and bromide combined with morphine or pethidine	Barbiturates	Gas and air only	Gas and air combined with morphine or pethidine	Chloroform (mask and drop-bottle)	General anæsthetic plus sedation		
Primip. under 20:											
Aided	..	..	..	..	..	..	..	..	1	..	1
Phys.	1	..	..	2	..	1	1	..	..	2	7
Primip. 20–24:											
Aided	..	..	..	..	..	..	..	..	5	..	5
Phys.	8	8	7	4	1	1	5	..	..	35	69
Multip. 20–24:											
Phys.	..	..	1	..	..	..	..	..	..	9	10
Primip. 25–29:											
Aided	..	..	1	..	..	1	1	1	13	..	17
Phys.	11	8	13	4	3	5	9	..	..	37	90
Multip. 25–29:											
Aided	..	..	..	..	..	..	..	..	2	..	2
Phys.	6	3	4	..	2	..	1	..	..	46	62
Primip. 30–34:											
Aided	..	..	..	..	..	..	..	1	16	..	17
Phys.	5	7	6	..	4	1	..	..	1	22	46
Multip. 30–34:											
Aided	..	..	..	..	..	..	..	..	1	..	1
Phys.	7	6	..	..	4	5	..	..	..	46	68
Primip. 35 or more:											
Aided	..	..	..	..	..	..	..	..	7	..	7
Phys.	2	4	1	..	4	..	1	..	..	12	24
Multip. 35 or more:											
Aided	..	..	..	..	..	..	..	..	2	..	2
Phys.	7	2	6	..	5	2	..	1	..	30	53
Total	47	38	39	10	23	16	18	3	48	239	481

Digitized by Google

TABLE V—COÖPERATION OF WOMEN IN LABOUR

Group	No. of cases	Coöperation		
		Good	Fair	Nil
Primip. under 20:				
Aided	1	..	..	1
Phys.	7	5	1	1
Primip. 20–24:				
Aided	5	3	1	1
Phys.	69	59	7	3
Multip. 20–24:				
Phys.	10	10	..	..
Primip. 25–29:				
Aided	17	4	4	9
Phys.	90	73	10	7
Multip. 25–29:				
Aided	2	..	1	1
Phys.	62	53	8	1
Primip. 30–34:				
Aided	17	2	6	9
Phys.	46	38	4	4
Multip. 30–34:				
Aided	1	..	1	..
Phys.	68	62	4	2
Primip. 35 or more:				
Aided	7	..	2	5
Phys.	24	20	1	3
Multip. 35 or more:				
Aided	2	1	..	1
Phys.	53	45	1	7
Total	481	375 (78%)	51 (11%)	55 (11%)

BIRTH WEIGHTS

The average weight of the babies in this series is interesting for the uniformity of all groups and the relatively high average:

	Of primiparæ	*Of multiparæ*	*Total*
Males	7 lb. 8 oz.	7 lb. 10 oz.	7 lb. 9 oz.
Females	7 lb. 7 oz.	7 lb. 8 oz.	7 lb. 7·4 oz.

The women in this series were all given printed diet sheets designed to maintain a balanced and restricted intake. It is difficult to estimate how many adhered to this advice. The time-worn question arises: "Does the mother's diet influence the size of the baby?" Apart from congenital predisposition, it is possible that maternal intake may control the development of her child, but can the average pregnant woman control the development of her appetite?

LENGTH OF GESTATION

The gestation period of 474 cases in which it was accurately recorded averaged 40 weeks, estimated from the first day of the last normal menses to the day of birth. The actual range was from 250 to 310 days.

COÖPERATION OF WOMEN IN LABOUR

An analysis of the amount of coöperation given by the mothers in labour is detailed in table v. Coöperation largely depended on antenatal preparation: (1) education in and understanding of the processes of pregnancy and labour; (2) the ability to relax during first-stage contractions and between second-stage contractions; and (3) physical preparation by a few simple exercises designed to give full, free, and controlled respiratory movements, mobility of pelvic joints, and general muscular fitness. During labour assistance in the application of this preparation should be given, and the woman reminded of the personal virtues of patience, self-control, and ability to work hard. This approach to labour, which is acceptable to most women of all social, economic, and educational classes, was construed with a care and conduct of labour based on an understanding of the physiological, emotional, and physical phenomena.

The 375 mothers who coöperated well were all offered analgesia and knew how to use the apparatus, which was by their left hand to use at will. None of them wished to use it, many resented the suggestion. All watched their babies born and most of them held the infant's hand before the sex was known, owing to the manner and position of delivery. In all cases the baby, adequately wrapped, was given to the mother as soon as the cord had been severed. Some mothers (not accurately recorded) put the baby to the breast at once, with a salutary influence on uterine contractions and placental separation. The unrestrained happiness of the good coöperator at the birth of her child is not only a delight to witness but also has an important physiological and emotional significance. In many cases the husband and the wife took tea together, mutually happy, with the newborn infant beside them within ten minutes of the expulsion of the placenta. In this series there has been no evidence of infection of babies by the attentions of their parents, but considerable evidence of benefit from the unrestricted interest (within reason) of a proud husband and father.

About a third of the good coöperators had a sedative at the first emotional menace, which enabled them to establish complete control throughout the rest of labour.

TABLE VI—BREAST-FEEDING AND GROWTH OF BABY

Group	No. of cases	Breast-feeding			No. of babies breast-fed	Weight of baby at 12 days in relation to birth weight		
		Good	Fair	Poor		Above	Same	Below
Primip. under 20:								
Aided	1	1	..	..	1	..	1	..
Phys.	7	5	1	1	7	3	..	4
Primip. 20–24:								
Aided	5	4	..	1	5	2	..	3
Phys.	69	46	14	9	68	37	7	25
Multip. 20–24:								
Phys.	10	7	3	..	10	5	1	4
Primip. 25–29:								
Aided	17	10	4	3	16	9	1	7
Phys.	90	47	25	18	90	33	10	47
Multip. 25–29:								
Aided	2	1	..	1	2	1	..	1
Phys.	62	34	23	5	62	27	3	32
Primip. 30–34:								
Aided	17	14	2	1	16	14	..	3
Phys.	46	27	14	5	46	21	2	23
Multip. 30–34:								
Aided	1	1	..	..	1	1	..	..
Phys.	68	35	22	11	65	26	8	34
Primip. 35 or more:								
Aided	6*	4	1	1	6	2	1	3
Phys.	24	20	2	2	23	17	2	5
Multip. 35 or more:								
Aided	2	1	..	1	2	1	..	1
Phys.	53	30	12	11	51	21	4	28
Total	480	287 (60%)	123 (26%)	70 (15%)	471 (98%)	220 (46%)	40 (8%)	220 (46%)

* 1 case omitted.

Digitized by Google

The mothers included as fair coöperators did not maintain complete control at one or other of the menaces —usually the second (at transition)—or the fourth (at early crowning). They required a repetition of sedative or a spell of analgesia, but all were conscious of, and fully awake to, the birth of the child.

The non-coöperators were mentally or constitutionally unable to carry out the procedures or had a low pain threshold, which was raised by early and protracted sedation or analgesia, and in complicated cases by deep anæsthesia for the birth of the child.

BREAST-FEEDING

The breast-feeding of the babies and their weights at 12 days in relation to their birth weights are given in table VI.

All the women in this series had antenatal preparation of the breasts according to the methods advocated by Waller. In the 9 cases in which the babies were not breast-fed, 4 mothers were mentally unsuited and refused to give the breast because they considered breast-feeding "disgusting," 3 had deformed breasts or nipples and were unable to feed, and 2 could not feed their babies because of their employment and being self-supporting

TABLE VII—DISTRIBUTION OF MULTIPARITY

Age-group (yr.)	No. of previous children			
	1	2	3	Total
Under 20 ..	0	0	0	0
20–24	10	0	0	10
25–29	57	6	1	64
30–34	41	21	7	69
35 or more ..	29	19	7	55
Total ..	137 (69%)	46 (23%)	15 (8%)	198

could not give up their jobs. In 471 cases (98%) the babies were entirely breast-fed on leaving hospital. The progress of the breast-fed babies up to 6 months was most satisfactory. Those breast-fed for 3 months only gave more weaning troubles than did those who continued for 6–9 months. The weight at 12 days of age in relation to birth weight in breast-fed babies is not of great significance. Many of the slow but healthy starters went ahead strongly when the mother returned home; this was especially so with multiparæ who were anxious about husband and family left at home while the mothers were in hospital. Giving complementary feeds to babies who are slow starters ("Fair" in table) is in most cases a mistake. Recent investigation points to the inadvisability of giving complementary feeds as a routine. Let the baby and the breast work out their own salvation; they usually succeed if not interfered with too much.

Of 124 multiparous women over the age of 29 years only 14 had had 3 previous children. It is perhaps the province of the eugenist to draw conclusions from these striking figures. If this is a fair sample—and the series is comprised of women from all walks of life and does not represent any particular social or financial group—the survival chance of our people is small. It points to the trend of society towards late marriages and small families. The social and domestic organisation prevailing under our present economic system is responsible to a great extent for the lack of births to parents who would have them willingly if homes and help were available. They want more children but dare not have them. Many have one child only, and no more are forthcoming because of the fear of childbirth and because of the suffering both mental and physical, that their child occasioned. In spite of this a considerable number of women decided to have more children when they read of physiological labour. It gave them confidence that their previous

TABLE VIII—ANALYSIS OF THE 52 FORCEPS DELIVERIES

Occipito-anterior presentation, no disproportion	Occipito-anterior presentation, some relative disproportion	Transverse arrest of head in mid cavity	Persistent occipito-posterior presentation	Coöperation and control			Coöperation and control not recorded	
				Good	Fair	Nil	Fœtal distress	Ill patients
22	5	7	18	17	5	21	3	6

experience would not be repeated. A high percentage of success justified their faith.

FORCEPS DELIVERIES

The 52 forceps deliveries are analysed in table VIII. Of the 27 occipito-anterior presentations, 16 women were emotionally abnormal, exhibiting complete lack of self-control from early labour. Of the 17 women who coöperated well and maintained self-control in spite of their abnormality, 13 expressed disappointment when told that interference was indicated, some requested to be allowed to go on trying, and 4 wept when told they would not see the baby born. The fair coöperators were those who broke down at the third or fourth menace.

Of the 6 ill women, 1 had been in bed for three months with pyelonephrosis, 2 had toxæmia of pregnancy with hyperpiesia, and 3 had been mentally unstable for some years and had been treated in mental homes.

In 26 of the 52 cases there was an emotional breakdown. Early delivery of these cases is indicated because of the high incidence of postnatal psychopathies if the women are left to complete a long second stage. They are given sedatives sufficient to maintain sleep for 6–8 hours after labour. Analgesia is insufficient to prevent psychological changes after the puerperium.

Of these 52 cases, only 1 baby suffered injury. It was a remaining twin, the other having miscarried at 11 weeks. The labour was of an ill mother with a first stage lasting 43 hours. Fœtus distress was diagnosed at four-fifths dilatation. Extraction with forceps lasted 10 min. after full dilatation. It was an easy delivery with no marks of external injury. The baby died a few hours later. Necropsy showed that a subtentorial hæmorrhage was the cause of death.

It should be noted that 34 of the 52 forceps cases were in primiparæ aged 27–34 years. For many years it has been noted that of the three 8-year periods from 19 to 42 the middle octad presents the greatest number of difficult labours in primiparæ. The causes are found in the emotional rather than the physical limitations.

CÆSAREAN SECTION

In ordinary circumstances an incidence of 28 cæsarean sections in 516 cases of labour (5·4% of all deliveries) would demand explanation. Probably there was a high proportion of borderline cases among the women who came for physiological childbirth, and those who had experienced difficulty or cæsarean section came under my care. They came hopefully, requesting that natural procedures might be given a fair chance in spite of previous cæsarean sections or clinical indications of physical limitation. This series is therefore a self-selected rather than average group. Thus 31 women (18 primiparæ and 13 multiparæ) presented themselves with these considerations in their minds. The primiparæ had all been diagnosed "small," either clinically or radiologically. Generally contracted or deformed pelves were found in 6 of the 18 primiparæ, and cæsarean section was performed; 2 had forceps delivery and 10 had physiological labour. The 13 multiparæ had all had cæsarean section for their first and only child. Of these, 7 had had a febrile puerperium and untrustworthy scars, and a second cæsarean section was performed;

Digitized by Google

1 had a deformed pelvis and gross disproportion—she also had a second cæsarean section—4 had easy physiological labour and 1 a low-forceps (Wrigley's) delivery.

A small woman had had 2 cæsarean babies, but was adamant that she could "do it properly." I found no clinical contra-indication, and her third baby was born of an easy natural labour, without analgesia or laceration. The infant weighed 8 lb. 13 oz., which was 1 lb. 2 oz. heavier than either of the others. Her previous children had been produced before labour began, because of her "small" size.

In 2 cases elderly primiparæ were mentally abnormal and so obsessed with the horrors of labour that it was decided to avoid the risk of serious breakdown. Diabetes mellitus, antepartum hæmorrhage, and acute toxæmia were the reasons for the remaining 7 cæsarean sections.

This general survey suggests that the advice to have cæsarean section is not always based on wide clinical experience. It is, however, an easy and relatively safe way for a good gynæcologist to produce a baby. It is a safer and more desirable operation than high forceps in a primipara with a small birth canal. But the women who had natural labours after previous cæsarean sections expressed intense satisfaction at their achievement. Perhaps even this small number of cases justifies the conclusion that great care should be exercised before assuming that physiological delivery is impossible. (With one or two exceptions these operations were lower-segment cæsareans performed by Mr. L. G. Higgins, F.R.C.S.)

CONCLUSIONS

Childbirth is a physiological function, not a pathological state. It is the serious test of a woman's fitness for motherhood which is of biological and sociological significance. Most women who are taught how, and assisted, to perform this natural test neither need nor desire drugs or anæsthetics.

The integrity of the physical mechanism of eutocia varies as the integrity of the emotional phenomena. The emotion of fear increases tension, disturbs stimulus interpretation, and so causes pain in otherwise normal labour. The understanding and care of the emotions avoid pain in labour and so protect both mother and child from dangers associated with interference.

The length of all stages of labour in this series is considerably shorter than the average given by De Lee (1938).

A conscious and controlled woman can assist in preserving the perineum from serious injury.

Fondling or suckling of a baby by the mother immediately after its birth, combined with a rational conduct of the third stage of labour, minimises the loss of blood, and the mothers get up on the third or fourth day after labour.

Sedatives and analgesics should be freely offered for emotional or physical disturbances during labour, but never given against the wish of the woman.

The "effort syndrome" is commonly mistaken for pain.

The antenatal diet of women of all classes should be a subject of instruction and serious advice.

No woman can coöperate in labour if she is left alone to "get on with it."

Practically all women having physiological labour wish to breast-feed their babies and do so successfully.

A rapid recovery to birth weight is not an indication of the ultimate well-being of a baby. Many slow starters make normal progress after the mother leaves hospital and ceases to worry about home affairs.

In this series, taken from all walks of life, the late breeding-age and the small size of the families should alarm the birth-rate statisticians.

The outstanding impression gained from the women in this series is the absence of all aversion to parturition. They speak of the supreme happiness of childbirth. Their euphoria is without design. They desire to repeat the experience as soon as the economic and domestic difficulties of our present social disorganisation make possible the housing and upbringing of another child.

Finally, it has become apparent that the woman of today demands to be taught how to have a healthy baby in a healthy way. She wishes to collaborate so far as possible in this achievement.

REFERENCES

De Lee, J. B. (1938) Principles and Practice of Obstetrics. 7th ed., Philadelphia and London.
Read, G. D. (1933) Natural Childbirth. London.
— (1942) Revelation of Childbirth. London.
— (1946a) *J. Obstet. Gynæc.* **53**, 55.
— (1946b) *Hlth Educ. J.* **4**, 131.
— (1947) Birth of a Child. London.
Sawyer, B. (1946) *Amer. J. Obstet. Gynec.* **51**, 852.

CURARE-LIKE ACTIONS OF TRI-(DIETHYLAMINOETHOXY)-BENZENE TRIETHYLIODIDE

WILLIAM W. MUSHIN
M.A. Oxfd, M.B. Lond., F.F.A., D.A.
DIRECTOR, DEPARTMENT OF ANÆSTHETICS, WELSH NATIONAL SCHOOL OF MEDICINE, CARDIFF

R. WIEN B.Pharm., Ph.C., D.B.A., Ph.D. Lond.
D. F. J. MASON B.Sc. Lond.
G. T. LANGSTON
BIOLOGICAL DIVISION, MAY & BAKER LTD., LONDON

SOME experiments on animals with tri-(diethylaminoethoxy)-benzene triethyliodide or R.P. 3697, now called 'Flaxedil,' have already been described (Bovet et al. 1946, 1947, Wien 1948a). A preliminary clinical account has also been given by Huguenard (1948). We describe here our recent pharmacological findings and the results of the first clinical experiments in this country.

PHARMACOLOGY

The action of flaxedil is like that of curare, inhibiting the transmission of nervous impulses by acetylcholine and blocking transmission across the myoneural junction of voluntary muscle. These effects are easily reversed by neostigmine ('Prostigmin') or by physostigmine. Flaxedil differs from *d*-tubocurarine chloride in having little paralysing action on autonomic ganglia. Its main pharmacological properties may be summarised as follows:

(1) Though it is less potent, weight for weight, than *d*-tubocurarine, this of itself is of little significance; the relation of its curarising potency to the effect on respiration must be taken into account. An ideal curarising agent should be relatively non-toxic, and it should be possible to give many times the paralysing dose with eventual recovery, provided artificial respiration is given.

Assays by the rabbit head-drop method indicated that flaxedil was about a third as potent as *d*-tubocurarine. After a dose producing head-drop for 5 min. the respiration was almost unchanged. With higher doses paralysis of the neck muscles and limbs was followed by paralysis of the intercostal muscles, respiration being maintained by the diaphragm; excessive doses inhibited respiration. In the rabbit flaxedil has about the same margin of safety as *d*-tubocurarine. The dose needed to arrest respiration was about 1·7 times the curarising dose, and the ratio for *d*-tubocurarine was 1·5. Previous injection of *d*-tubocurarine sensitises animals to flaxedil, and account must be taken of this.

(2) The neuromuscular blocking effects of flaxedil are easily reversible by prostigmin or by physostigmine. This is demonstrable in the rabbit phrenic-nerve diaphragm preparation (Wien 1948b) and strikingly in man (figs. 4 and 6). Unlike some synthetic curarising agents, flaxedil has no eserine-like properties. It slightly stimulates isolated rabbit gut but only in comparatively high concentrations.

(3) No vasodepressor effect is caused, even with many times the paralysing dose, provided there is adequate oxygenation. The injection of 2 mg. of flaxedil into the arterial supply

Digitized by Google

of a dog's hind-limb perfused with heparinised blood had no effect, whereas 1 mg. of *d*-tubocurarine chloride produced a slight fall of pressure and dilatation of the vessels.

(4) Experiments on isolated tissues (rat diaphragms) showed that flaxedil liberated less histamine ($^1/_6$–$^1/_2$) than did *d*-tubocurarine.

(5) Flaxedil has but little paralysing action on ganglia. This was shown in anæsthetised cats, in which the contractions of the nictitating membrane were recorded by stimulation of the preganglionic fibres of the cervical sympathetic nerves. Whereas the intravenous injection of 1 mg. of *d*-tubocurarine caused pronounced inhibition, 100 mg. of flaxedil had only a slight effect; this confirmed an observation of Depierre (1947).

We investigated whether flaxedil had any sparing effect on the respiration. We had observed, in conscious animals and in man, that complete paralysis of certain voluntary muscles could be obtained without unduly affecting the respiration. In cats under light pentobarbital anæsthesia, when the corneal reflexes could be briskly elicited, it was possible with an intravenous injection of flaxedil to paralyse almost completely the gastrocnemius muscle, without much affecting the respiratory ventilation (fig. 1). Though the intercostal muscles were paralysed, respiration was efficiently carried on by movements of the diaphragm. To analyse this effect graded doses of *d*-tubocurarine and of flaxedil were injected intravenously and the paralysis of the gastrocnemius was compared with the depression of the respiration (fig. 2). A comparison of the dose just causing complete paralysis with that just arresting respiration (10% of normal or 90% paralysis) indicated the margin of safety or sparing action on the respiration. For flaxedil the doses were respectively 0·45 and 0·86 mg. per kg. of body-weight (ratio 1·9), and for *d*-tubocurarine chloride 0·2 and 0·34 mg. (ratio 1·7). For C_{10}, bistrimethyl-ammonium decane (Paton and Zaimis 1948), the respective doses were 0·053 and 0·13 mg. per kg. of body-weight (ratio 2·45). At the dose just causing 100% paralysis of the gastrocnemius the respiratory ventilation was 25% of the normal for *d*-tubocurarine, 30% for flaxedil, and 45% for C_{10}. Because the previous injection of *d*-tubocurarine enhanced the effect of a subsequent injection of flaxedil and antagonised that of C_{10}, each compound was used separately in each experiment. A paralysing dose of flaxedil had a slightly shorter action, about 20 minutes before full recovery compared with 30 minutes for *d*-tubocurarine.

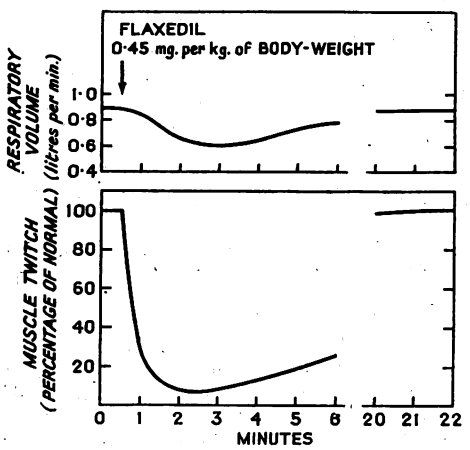


Fig. 1—Cat. Pentobarbital anæsthesia. Lower record of gastrocnemius twitch tension elicited by stimulation of sciatic nerve every 4 sec. with maximal induction shocks; upper record of respiratory volume (Gaddum's method). Flaxedil injected intravenously.

EFFECTS OF FLAXEDIL IN CONSCIOUS PERSONS

Experiments were made on conscious volunteers to obtain quantitative data. Initially, electromyographic observations with a cathode-ray oscilloscope and amplifier were made. Numerous difficulties were met in obtaining records of muscle activity and in interpreting them to obtain quantitative measurements. The contracting power of certain muscles was more readily measured with mechanical devices. On command, the volunteer made his greatest effort to perform the desired movement, and the power of the muscle or group of muscles involved was read on a scale attached to the mechanical device. Observations were made every half minute. Flaxedil was slowly injected intravenously and muscle power observed. If complete paralysis was not produced, more flaxedil was immediately given until the desired effect was obtained. The subjective sensations of the volunteers are not set out here because they tallied closely with those already described for *d*-tubocurarine. Seven volunteers submitted to more than one experiment. In one volunteer *d*-tubocurarine was given in one experiment and flaxedil in another, so that the two drugs could be compared in the same person. The antagonising effect of prostigmin was also observed.

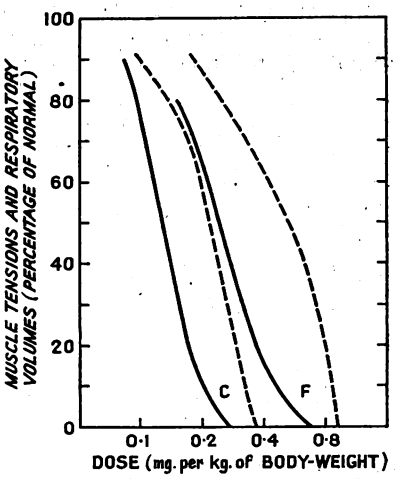


Fig. 2—Record of gastrocnemius tensions (continuous lines) and respiratory volumes (interrupted lines) in cats under light pentobarbital anæsthesia: C, *d*-tubocurarine chloride; F, flaxedil injected intravenously. Logarithmic dose scale. See text.

The observations made were:

(1) Power to flex the fingers: a dynamometer was constructed in which a pointer moved over a graduated scale and showed "flexing power."

(2) Power to contract the recti abdominis muscles: the volunteer lay supine with knees firmly strapped down; a spring-loaded pad bore on the centre of the recti abdominis; on the command "Raise your legs," the recti became taut, and the pad was pushed upwards against a spring which moved a pointer over a scale.

(3) Respiration was recorded with a spirometer, and the ventilation over 1 min. periods was calculated from the record obtained.

(4) The movements of the diaphragm were recorded on a fluorescent screen in two cases by a technique devised by members of the Medical Research Council's Pneumoconiosis Research Unit at Llandough, Cardiff.

(5) Blood-pressure.

(6) The plantar reflex was tested at short intervals to demonstrate reflex activity unrelated to conscious effort.

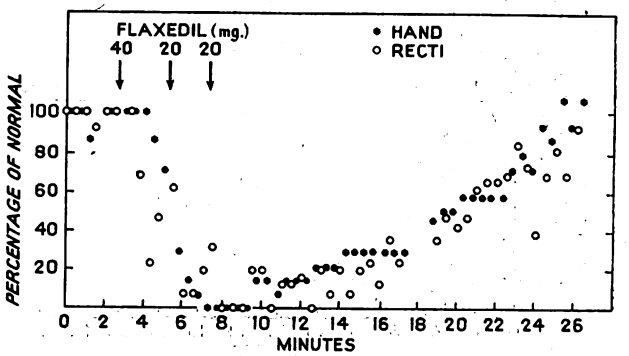


Fig. 3—Record of "flexing power" of fingers, and power to contract recti abdominis muscles in a volunteer. Flaxedil injected intravenously.

Digitized by Google

The main results may be summarised as follows:

(1) In doses of 40–70 mg. (about 1 mg. per kg. of body-weight) injected intravenously in conscious persons, complete paralysis of the flexor muscles of the forearm and of the muscles of the abdominal wall developed within 4 min.

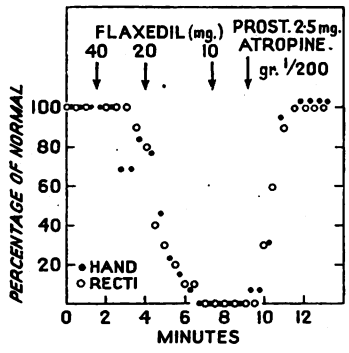


Fig. 4—Similar records to fig. 3 in a further volunteer. Note quicker recovery after prostigmin.

(2) The paralysis so induced passed off in about 25 min. (fig. 3), leaving strikingly few after-effects.

(3) At this dosage there was no demonstrable decrease in pulmonary ventilation (figs. 5 and 6), though some of the volunteers, who were doctors, reported that intercostal breathing was interfered with. The absence of any effect on the diaphragm was confirmed by recording the movements of the diaphragm in some experiments. In only one person was there hyperventilation during the time of greatest paralysis (fig. 5). This appeared to us to be due to apprehension. This person also showed hyperventilation in a subsequent and similar experiment with *d*-tubocurarine.

(4) The paralysis induced by flaxedil was completely and rapidly neutralised by an intravenous injection of prostigmin (figs. 4 and 6), which restored full muscular power in about 10 min. The recovery was so complete that the volunteers could immediately assist with other experiments.

(5) The blood-pressure showed no pronounced alteration.

(6) When no power remained in the flexor muscles of the forearm, the sole of the foot was stroked, and no reflex was elicited. At this moment the jaw was relaxed and required support.

(7) Sweating was not marked and none of the volunteers became cyanosed, though no assistance was given to respiration.

(8) Dosage: about 1 mg. per kg. of body-weight was the paralysing dose in conscious men. Experiments are in progress to determine the dose which just stops respiration, so that the ratio discussed above for animals can be calculated for man.

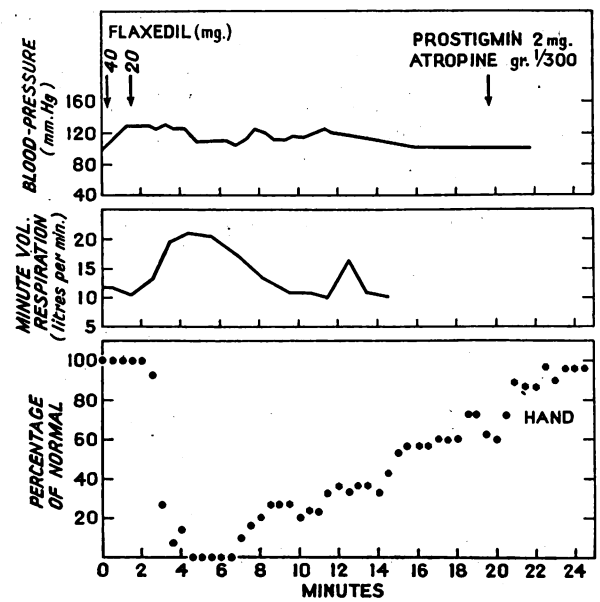


Fig. 5—Record of "flexing power" of fingers, pulmonary ventilation, and blood-pressure in a volunteer. Flaxedil injected intravenously.

Flaxedil has also been used during light cyclopropane and ether anæsthesia in 45 adult patients to paralyse the abdominal wall during major abdominal operations. In most cases it was necessary to give up to a total of 100–120 mg. Usually two doses were necessary, the first one wearing off after about half an hour. From experience with *d*-tubocurarine in similar circumstances the effect of 80 mg. of flaxedil was roughly equivalent to about 15 mg. of 'Tubarine.'

We have confirmed its speedy elimination in anæsthetised and artificially respired rabbits and cats which, given 3–10 times the curarising dose, excreted within 2 hours from 30–100% in the urine (assayed on the rabbit phrenic-nerve diaphragm preparation).

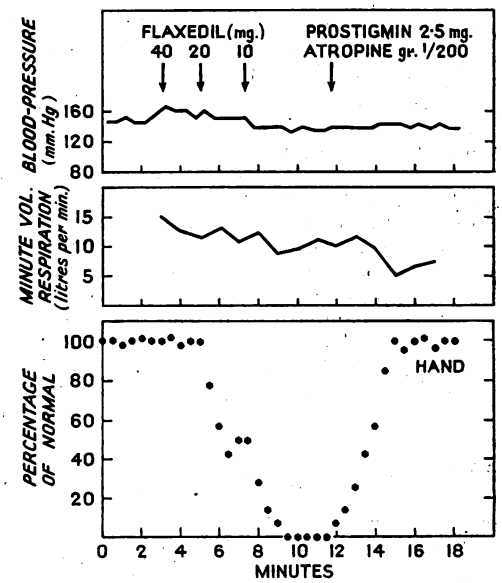


Fig. 6—Similar records to fig. 5 in a further volunteer. Note quicker recovery after prostigmin.

CONCLUSION

Flaxedil is an effective curarising agent. It is a stable and easily prepared synthetic compound, soluble in water, and aqueous solutions are miscible with those of thiopentone sodium. Though it is less potent than *d*-tubocurarine, the fact that the ratio of the paralysing dose to the dose arresting respiration is similar to that of *d*-tubocurarine is more significant. Moreover, flaxedil produces a neuromuscular block which is readily antagonised by the anticholinesterases prostigmin and physostigmine. Investigations so far have revealed no side-effects. In animals and in man, provided there is adequate oxygenation, there is no depressant effect on the blood-pressure. In conscious men, in doses that just caused complete paralysis of the abdominal and forearm muscles, pulmonary ventilation was unimpaired, movements of the diaphragm being unaffected. The duration of action of flaxedil is slightly less than that of *d*-tubocurarine; recovery is rapid and complete in a conscious person within 30 min. of a full paralysing dose.

We are much indebted to the volunteers, and also to Mr. D. Ezard, who constructed the mechanical devices.

REFERENCES

Bovet, D., Courvoisier, S., Ducrot, R., Horclois, R. (1946) *C.R. Acad. Sci., Paris*, **223**, 597.
— Depierre, F., de Lestrange, Y. (1947) *Ibid*, **225**, 74.
Depierre, F. (1947) *Ibid*, p. 956.
Huguenard, P. (1948) communication to International Congress of Medicine, Ostend, Sept. 5.
Paton, W. D. M., Zaimis, E. J. (1948) *Nature, Lond.* **162**, 810.
Wien, R. (1948a) *Arch. int. Pharmacodyn.* **77**, 96.
— (1948b) *J. Physiol.* **107**, 44P.

Digitized by Google

STREPTOMYCIN IN NON-TUBERCULOUS INFECTIONS *

P. H. BUXTON
M.B. Camb.
MEDICAL REGISTRAR

ROSEMARY D. SIMON F. R. SELBIE
B.Sc., Ph.D.Lond. M.A., M.D.Aberd., D.Sc., Ph.D.Lond.
ASSISTANT PATHOLOGISTS, BLAND-SUTTON INSTITUTE OF PATHOLOGY
MIDDLESEX HOSPITAL

IN January, 1947, the Middlesex Hospital was invited by the Streptomycin Clinical Trials (Non-tuberculous Conditions) Committee of the Medical Research Council to form one of the centres for investigating the value of streptomycin in the treatment of non-tuberculous infections. This report presents the results up to August, 1948, when 67 cases had been treated comprising the following conditions:

(1) 44 cases of urinary infection, chiefly by *Ps. pyocyanea* and *Bact. coli*;
(2) 14 cases of wound infection, mainly by *Staph. pyogenes*;
(3) 9 miscellaneous infections.

Streptomycin was given only to patients in whom the infecting organism had been proved in vitro to be sensitive to streptomycin but insensitive to penicillin and the sulphonamides.

METHODS OF ADMINISTRATION AND MANAGEMENT

At the start of this investigation streptomycin was given intramuscularly every 3 hours. After the first 20 patients had been treated, the same daily dosage was given 4-hourly, since this proved effective in maintaining therapeutic blood-levels and was less disturbing to the patient. In children the daily dosage was 20 mg. per lb. of body-weight. A short course of treatment with a high initial dosage was considered unlikely to give rise to toxic symptoms, and more likely to be effective in preventing the development of bacterial resistance, than a protracted course with low dosage. The patients with wound infection were usually given 4 g. daily for 2 days to obtain a high concentration of streptomycin in the tissues rapidly. The dosage was then reduced to 2 g. daily, which usually sufficed to control these wound infections.

The dosage generally used in urinary infections was 3 g. daily for a 4-day course. This was obtained by diluting the 1 g. ampoules of streptomycin salt with 4 ml. of pyrogen-free distilled water to produce a 1 in 4 (25%) solution; 2 ml. of this solution was injected 4-hourly. If there was much pain at the site of injection, the 1 in 4 solution was obtained by using 1 ml. of 1% procaine and 3 ml. of distilled water for diluting each 1 g. ampoule.

Streptomycin was given locally by insufflation as well as systemically in cases of superficial infections. Owing to the narrow range of bacteria sensitive to streptomycin, penicillin and sulphathiazole were added to the powder for insufflation as a precaution against accidental contamination of the wound, during dressings, with organisms resistant to streptomycin but sensitive to penicillin and sulphonamides.

The proportions used in the powder were streptomycin 1 g., penicillin 45,000 units, and sulphathiazole 9 g. There appeared to be no interference with the normal healing of the wound when this powder was administered by insufflation every 3 or 4 hours to give a total daily dosage equivalent to 1 g. of streptomycin.

Streptomycin was given by subconjunctival injection as well as systemically in cases of panophthalmitis. The subconjunctival dose was given in 6 minims (0·4 ml.) of water; 1 mg. was given on the first day, and 30 mg. on each of the next 3 days. There was no undue local reaction. In a later case of hypopyon subconjunctival doses of 200 mg. in 6 minims of distilled water were well tolerated.

In the cases of urinary infection potassium citrate was given during treatment to keep the urine alkaline, since it was confirmed by preliminary bacteriological investigations that streptomycin was more effective in an alkaline medium. Fluids were not restricted, though it has been suggested that restriction of fluids, by increasing the urinary concentration of streptomycin, may allow a reduction in dosage.

Patients with suprapubic drainage and a bladder containing thick pus and debris had, in addition to the intramuscular streptomycin, 3-hourly bladder washouts with sodium bicarbonate solution in a concentration of 1 in 160 (1 drachm to the pint); washouts were continued as long as was necessary to prevent obstruction to drainage. Streptomycin was not added to the solution for washouts, since adequate concentrations of the drug were already present in the urine.

The blood-urea was estimated in cases suspected of impaired renal function, since this condition has been reported to give an increased incidence of the more toxic symptoms, owing to the retention of high concentrations of streptomycin in the blood-stream (McDermott 1947). In a case of papillary carcinoma of the bladder with a *Ps. pyocyanea* urinary infection the blood-urea level was 80 mg. per 100 ml. at the start of treatment but fell to normal (30 mg. per 100 ml.) after a few days. On a dosage of 3·2 g. daily, this patient's blood-serum contained 32 μg. of streptomycin per ml. over the 3-hour period, a level no higher than that found in our other patients on the same dosage.

RESULTS

Urinary Infections

Table I summarises the results of streptomycin treatment in 44 cases of urinary infection. In this table all the patients who had suprapubic drainage during

TABLE I—URINARY INFECTIONS TREATED WITH STREPTOMYCIN

Condition at time of treatment	No. of cases	No. with mixed infection	No. infected at start of treatment					Clinical result		
			Ps. pyocyanea	*Bact. coli*	*Strep. fæcalis*	*Staph. pyogenes*	*Proteus*	Cured	Improved	No change
(*a*) Suprapubic drainage	10	8	8	3	5	2	3	1	3	6
(*b*) After prostatectomy	6	2	5	2	0	0	1	2	3	1
(*c*) New growth	10	2	8	1	1	1	1	2	3	5
(*d*) Operation other than (*b*) or (*c*) ..	2	0	2	0	0	0	0	0	0	2
(*e*) Acute or chronic infection	16	3	3	10	3	3	1	9	3	4
Total	44	15	26	16	9	6	6	14	12	18

* This work was done on behalf of the Streptomycin Committee of the Middlesex Hospital under the auspices of the Medical Research Council.

Digitized by Google

treatment are grouped together, whereas the others are classified according to clinical condition. It can be seen that about a third of the patients were cured, a third improved, and a third unchanged.

The criteria used for cure were sterile urine and absence of symptoms of infection. Patients were assessed as improved when the amount of pus in the urine was less or the clinical condition, judged by temperature or urinary symptoms, was alleviated.

Failures were caused to some extent by clinical conditions, a notable example being suprapubic drainage, which gave a high proportion of failures owing to inevitable reinfection. An equally important factor, however, appears to be the infecting organism, there being a higher proportion of failures in *Ps. pyocyanea* infection and with mixed infections. Though there is some correlation between the infecting organism and the result, there is no doubt that a high proportion of cases where treatment failed had either some obstruction in the urinary tract, or slough formation in the bladder, which prevented all the infecting organisms from being exposed to full concentrations of streptomycin.

There is no doubt that these factors have been the chief cause of failure in urinary infections treated with penicillin and the sulphonamides, but streptomycin therapy is often also complicated by a rapid development of drug-resistance by the infecting organisms. It is thus all the more important that any obstruction in the urinary tract should be dealt with where possible before treatment with streptomycin is started.

WOUND INFECTIONS

Of 14 patients treated 10 were cured, 2 were improved, and in 2 there was no change (table II).

CASE 53, assessed as improved, had an infected wound following surgical division of the clavicle. The discharge from the wound diminished during treatment, but the original infecting organism persisted. Streptomycin was stopped after the administration of 22 g. owing to the development of skin sensitivity to the drug. After treatment a sequestrum and fixation wire were removed from the wound, and it was thought that mechanical factors had prevented the streptomycin from reaching all foci of infection.

CASE 46, assessed as improved, had an infected skin wound after a Smithwick's operation. The discharge diminished during treatment, but streptomycin therapy was stopped because of a low-grade pyrexia which was thought to be due to the antibiotic; this was confirmed when streptomycin was omitted and the temperature returned to normal. The skin wound later healed uneventfully.

CASE 48, one of the patients whose condition after treatment was unchanged had a wound infection following thyroidectomy. The organism originally isolated was *Staph. pyogenes* sensitive to streptomycin and the sulphonamides but not to penicillin, and a course of sulphamerazine was therefore started. After 12 days' treatment associated with some clinical improvement, the sulphamerazine was stopped because the patient developed sulphonamide sensitivity. At the same time the organism was found to have remained sensitive to streptomycin only. A course of streptomycin was started, but after 4 days the infecting organism, *Staph. pyogenes*, became insensitive to this drug. It was thought in this case that the silk ligatures in the wound had been the mechanical factor sheltering the organism and allowing drug resistance to develop.

In the 10 cases assessed as cured the wounds healed rapidly after elimination of the infection by streptomycin.

Miscellaneous Infections

The results in this group are summarised in table III, but some brief notes of special interest are given below.

CASE 61, with aplastic anæmia, developed an infection of a blood-transfusion wound which was followed by multiple pyæmic abscesses. The clinical condition was deteriorating rapidly; there was a swinging temperature and a total white-cell count of only 2000 per c.mm. The infecting organism, *Staph. pyogenes*, which was cultured from the superficial lesions but never from the blood, was sensitive to streptomycin only, yet high dosage of the drug did not prevent a rapidly fatal termination.

CASE 62, with congenital subaortic stenosis, was admitted with subacute bacterial endocarditis. The clinical condition improved on large doses of penicillin, but the temperature did not settle, and there were signs of embolic nephritis. A course of sulphamerazine produced some further improvement, but signs of activity were still present. At this time *Hæmophilus para-influenzæ* was identified in a blood-culture. This organism fixed complement in the presence of the patient's serum and was sensitive to streptomycin. A course of streptomycin was started, and the patient's condition improved dramatically—the temperature settled and red cells disappeared from the urine. Streptomycin 0·4 g. 3-hourly was given for 20 days and then 0·5 g. 6-hourly for 22 days—

TABLE II—WOUND INFECTIONS TREATED WITH STREPTOMYCIN

Case no.	Condition	Original infecting organism	Course of streptomycin (days)	Total dose of streptomycin (g.)	Residual organism	Clinical results
45	Spinal fusion graft	*Staph. pyogenes*	20	60 S + 10 L	*Staph. pyogenes* *	No change
46	Smithwick's operation	,,	8	24 S	—	Improved
47	Appendicectomy and hæmorrhagic blood disorder	,,	9	13 SL	—	Cured
48	Thyroidectomy	,,	4	12·8 S	*Staph. pyogenes* *	No change
49	Panophthalmitis	,,	3	14 SL	—	Cured
50	Osteomyelitis ilii, with removal of infected bone	,,	14 7	27 S + 12 L 7 L	*Staph. pyogenes* *	Cured
51	Laryngectomy	,,	11	26·8 S	—	Cured
52	Spinal fusion graft	,,	5 7	15 S + 5 L 10 L	—	Cured
53	Removal of neurofibroma from brachial plexus	,,	8	21·8 S + 5 L	*Staph. pyogenes*	Improved
54	Mastectomy	,,	4	11·2 S	—	Cured
55	Recurrent infection of hand	,,	5	16 S	—	Cured
56	Empyema after gastrectomy	*Bact. coli* and *Staph. pyogenes*	23	69 S + 3 L	—	Cured
57	Infected burns	*Ps. pyocyanea*	11 10	27 S + 11 L 10 L	Several	Cured (grafts took well)
58	Mastectomy	*Proteus*	6	16 S	—	Cured

S, systemic only. L, local only. SL, systemic and local. * Showed increased resistance to streptomycin.

Digitized by Google

TABLE III—MISCELLANEOUS INFECTIONS TREATED WITH STREPTOMYCIN

Case no.	Diagnosis	Infecting organism	Course of streptomycin (days)	Total dose of streptomycin (g.)	Clinical result
59	Lung abscess	*Bact. friedlanderi*, *Ps. pyocyanea*	7	18 S	No change
60	Empyema	*Bact. friedlanderi*	20	49 S + 3 L	Improved; vestibular disorder
61	Aplastic anæmia, bacteræmia	*Staph. pyogenes*	16	45 S	Died
62	Subacute bact. endocarditis	*H. para-influenzæ*	44	108 S	Cured; vestibular disorder
63	Myeloid leukæmia	*Staph. pyogenes*	(i) 10 (ii) 16	21 S 30 S	(i) Improved (ii) Slight improvement
64	Pemphigus	*Staph. pyogenes*, *Strep. pyogenes*, varied	(i) 30 (ii) 18	69 SL 54 SL	(i) Improved (ii) No change
65	Mooren's ulcer	*Staph. pyogenes*	4	12 SL	No change
66	Rhinoscleroma	—	60	150 S	Much improved
67	Hypopyon	—	10 4	17 S 2 SL	Much improved

S, systemic only. SL, systemic and local.

a total of 108 g. in 6 weeks. The patient is now, 8 months later, well and working, but there is much impairment of vestibular function.

CASE 66 was a Polish soldier admitted with an extensive rhinoscleroma, confirmed by biopsy, involving the whole nasopharynx and extending down the trachea and larynx. Obstruction had necessitated tracheotomy 7 months previously. The patient then had courses of penicillin and deep X rays, with little objective improvement. A course of systemic streptomycin, 3 g. daily, was started. After a month the appearance of the mucosa improved, with subjective improvement in breathing. Vertigo had developed, and the dosage of streptomycin was therefore reduced to 2 g. daily. Giddiness became less troublesome, and 2 months after the start of streptomycin therapy the appearance of the nasopharynx had considerably improved. It was now possible to spigot the tracheotomy tube for several hours at a time. A total of 150 g. was given in 2 months. The result seems promising, but the patient is still under observation.

CASE 64 was a man of 47 with pemphigus vegetans. From the lesions a very varied bacterial flora had been cultured. The patient had responded well to penicillin in 1944 but had quickly relapsed. Other treatments had been tried, with temporary benefit. It was thought justifiable to give a course of streptomycin systemically and locally. There was immediate improvement followed by relapse, and the patient did not respond to a second course of streptomycin.

CASE 60, who had had a left lower lobectomy and lingulectomy for bronchiectasis, developed an empyema from which Friedlander's bacillus was cultured. A course of systemic streptomycin 3 g. daily was given; the empyema was aspirated daily, and streptomycin 0·5 g. in 1 ml. of distilled water was injected into the cavity. After 48 hours the fluid aspirated was clear and culture was sterile. After a week's treatment vertigo, tinnitus, and headache developed suddenly, and the dosage of streptomycin was reduced to 2 g. daily, followed by diminution of these symptoms. A total of 49 g. systemically and 5·5 g. locally was given, with much improvement in the chest condition; the vertigo, though considerably diminished, has persisted.

SIDE REACTIONS TO STREPTOMYCIN

No auditory symptoms were encountered in this series, but vestibular disturbance was well marked in 3 cases and transitory dizziness in 2 cases. In the latter 2 cases reduction in streptomycin dosage in one case and cessation of treatment in the other alleviated the symptoms. There were no permanent sequelæ. In 2 of the 3 cases in which vertigo was more severe symptoms did not arise till a month after treatment was started. However, in case 66, where the patient received 3 g. daily systemically and 1 g. daily into an empyema cavity, symptoms started abruptly after only a week's treatment. Quantitative caloric tests showed complete absence of labyrinthine response in this case. An interesting clinical feature was the finding of nystagmus in only 1 of these 5 cases.

In larger series of cases vestibular disturbance has been found in practically all cases after 3 or 4 weeks' treatment with a dosage of 2–3 g. daily (McDermott 1947). Higher dosage produced vestibular symptoms more rapidly. It is not yet known how permanent the vestibular changes are, but clinically there is usually compensation within 2–3 weeks, particularly in younger patients and when re-education by good physiotherapy is available. The residual symptom is difficulty in walking in the dark.

Less serious side reactions to streptomycin included pain at the site of injection in about 20% of cases; headache and nausea in about 10%, mostly in urinary cases receiving potassium citrate by mouth; skin rashes in 2 cases; drug pyrexia in one case; and circumoral paræsthesiæ in 3 cases.

Severe pain at the site of injection was encountered more often with the earlier batches of streptomycin. The pain developed after 2–3 days' treatment and was only temporarily relieved by the addition of procaine; it gradually passed off 3–4 days after the injections had been stopped. Pain was less often encountered when the drug was injected slowly and when the site of injection was varied. Once pain had developed it appeared to be a general hyperæsthesia to injections of streptomycin rather than a local reaction, since the same intensity of pain was experienced whatever the site of injection.

The skin rashes, which were of an irritating morbilliform type, rapidly responded to anti-histamine drugs. Contact dermatitis among the nurses giving the injections, as has been reported by Crofton and Foreman (1948), was not seen.

Circumoral paræsthesiæ, encountered in 3 cases, consisted in tingling round the lips and face, associated in one case with slight swelling of the lips. These symptoms were only transitory and developed within the first few days' treatment.

No gastro-intestinal symptoms, apart from slight nausea in a few cases, could be directly attributed to streptomycin.

It was considered that, when there was danger to life or rapid extension of infection by streptomycin-sensitive organisms, none of these side reactions was sufficiently serious to warrant cessation of treatment.

BACTERIOLOGY

The sensitivity to streptomycin of organisms isolated from cases before, during, and after streptomycin treatment and the concentration of streptomycin in blood and urine have been tested by the methods previously used for penicillin (Selbie et al. 1945) and by a plate method using discs of filter-paper.

Digitized by Google

Sensitivity to streptomycin has, where possible, been tested on a sweep from confluent growth to give the greatest possible chance of finding resistant organisms.

Streptomycin Sensitivity

The streptomycin sensitivity of the organisms isolated from the first 20 treated cases was estimated by the titration method. These organisms, comprising several strains each of *Ps. pyocyanea, Bact. coli, Proteus, Strep. fæcalis,* and *Staph. pyogenes,* were inhibited by streptomycin in concentrations of 0·5–32 μg. per ml., giving figures in good agreement with those collected from various observers by Murray et al. (1947).

Sensitivity, however, can be measured accurately enough for clinical purposes by the plate method, and this has been used to determine the sensitivity of organisms isolated from all later cases. All of the 74 strains isolated before treatment from the last 47 cases had a similar range of sensitivity to the organisms isolated from the first 20 cases.

The distribution of these organisms is given in table IV, with the number of strains of each species which persisted during treatment and of those which became resistant to streptomycin: 54 out of 94 strains persisted, and 34 of these became highly resistant (some of the resistant strains of *Ps. pyocyanea* withstood as much as 30,000 μg. per ml.); and 29 organisms other than the original

TABLE IV—DISTRIBUTION OF INFECTING ORGANISMS UNDER STREPTOMYCIN THERAPY, SHOWING NUMBER OF STRAINS STREPTOMYCIN RESISTANT AFTER TREATMENT.

Organism	No. of strains isolated before treatment	No. of residual strains of original species		No. of residual strains of other species	
		Resistant	Sensitive	Resistant	Sensitive
Ps. pyocyanea ..	29	14	7	10	6
Bact. coli ..	22	8	5	2	4
Proteus ..	4	0	1	2	1
Bact. friedlanderi	2	0	0	0	0
Strep. fæcalis ..	8	4	0	0	0
Strep. pyogenes	2	1	0	0	0
H. para-influenzæ	1	0	0	0	0
Staph. pyogenes	26	7	7	0	4
Total ..	94	34	20	14	15

species were isolated after treatment, almost half of which were resistant to streptomycin.

In 5 cases of urinary infection resistant strains of the same species as the original organism were isolated after 3 or more days during which the urine remained sterile. In one case of urinary infection (belonging to the tumour group and assessed as improved) cultures of *Ps. pyocyanea* were obtained before treatment and 9 days later, the only organism cultured during this interval being a streptomycin-resistant *Staph. pyogenes.* Both strains of *Ps. pyocyanea* were of the same phage type (Warner 1948), though the later strain was at least 500 times more resistant to streptomycin than the original strain.

STREPTOMYCIN CONTENT OF BLOOD AND URINE

Tests for streptomycin in the blood-serum of patients receiving 3-hourly intramuscular injections of streptomycin 0·4 g. showed that the bacteriostatic levels of the serum were equivalent to 16–64 μg. of streptomycin during the first 2 hours, and to 8–64 μg. at 3 hours after injection.

Table V shows that the streptomycin content of 39 samples of urine from 14 patients on a daily dosage of streptomycin 3·2 g. varied considerably. In two-

TABLE V—STREPTOMYCIN CONTENT OF URINE DURING COURSES OF INTRAMUSCULAR STREPTOMYCIN 0·4 G. 3-HOURLY.

No. of urine samples with a bacteriostatic level equivalent to a concentration of streptomycin (μg. per ml.)		
250–500	1000–2000	8000–50,000
13	21	5

thirds of the samples the streptomycin content was at least 1000 μg. per ml., and the sample with the lowest bacteriostatic level contained 250 μg. per ml., a concentration at least ten times that necessary to inhibit the growth of most infecting organisms. These high concentrations of streptomycin in the urine, however, were insufficient to prevent the rapid development of resistant strains of bacteria, particularly in infections with *Ps. pyocyanea.* Of the 5 samples of urine containing at least 8000 μg. per ml. of streptomycin, 3 were obtained from a case of urinary infection in which *Ps. pyocyanea* was quickly eliminated from the urine but reappeared four months later as a highly resistant strain.

DISCUSSION

In the wound infections the results of streptomycin therapy were promising. Organisms highly insensitive to penicillin and the sulphonamides were, in our cases, highly sensitive to streptomycin; and, provided that the wound was freely drained surgically, rapid improvement was obtained with streptomycin. Decrease in the discharge and diminution in constitutional symptoms were noted usually within a day or two of starting treatment, and the wound became sterile usually within a week. A few cases improved clinically, though the infecting organism persisted in the wound. All our patients with infected wounds received systemic streptomycin, and where there were exposed surfaces, from which reasonable absorption of the drug could be expected local treatment was also given. Treatment was continued till the wound was sealed with healthy granulation tissue and discharge had ceased, or till a streptomycin-resistant organism was cultured from it.

In the urinary infections all patients in whom the infecting organisms were eliminated had sterile urine within 72 hours, and usually within 24 hours, of starting treatment; any organisms still present after 72 hours showed greatly reduced sensitivity to streptomycin. It was therefore concluded that no advantage was gained by giving streptomycin in adequate dosage for longer than 4 days in urinary infections, except in the rare event of the residual organism remaining sensitive to the drug. Thus in cases with suprapubic drainage only temporary sterilisation of the urine should be expected because of inevitable reinfection.

Possibly the resistant strains of *Ps. pyocyanea* found during and after streptomycin treatment of these cases may be reinfections, but it is much more likely that they are the original strains of infecting organisms which have become resistant because they have been insufficiently accessible to the streptomycin, since the resistance found has been well beyond the range of resistance of naturally occurring strains. Also, in the only case in which *Ps. pyocyanea* was phage typed, the original sensitive strain and final streptomycin-resistant strain were found to be of the same type.

The blood-streptomycin levels are very much lower than blood-penicillin levels in relation to the sensitivity of the infecting organism, but they are generally several times greater than the bacteriostatic dose required for the infecting organisms, and are evenly maintained over the whole period between injections, whereas with penicillin a high peak is followed by a rapid fall.

It has, however, been our experience with penicillin that even during several weeks' treatment no infecting

Digitized by Google

organism has developed sufficient resistance to become insensitive to increased doses of penicillin, but with streptomycin the resistance developed in a few days has been far beyond the range of streptomycin treatment, since the dosage, already bordering on toxic levels, cannot be sufficiently increased without endangering the patient.

It is therefore even more important with streptomycin than with the sulphonamides and penicillin that, when treatment is started, the largest possible dose consistent with the safety of the patient should be given.

SUMMARY

Streptomycin was given in 67 cases of infection by organisms insensitive to the sulphonamides and penicillin but sensitive to streptomycin.

Relatively large doses of streptomycin limited to a 4-day course in urinary infections due to a susceptible organism are likely to cure about a third of the cases, provided there is no mechanical obstruction to drainage producing an inaccessible nidus of infection.

In staphylococcal infections resistant to other forms of chemotherapy the use of streptomycin has been promising. If no improvement occurs within a week of starting streptomycin, further treatment by surgery to eliminate inaccessible foci of infection and provide adequate drainage should be considered.

Side reactions to streptomycin were encountered in less than a third of the cases, and in only 3 cases, where there was severe vestibular disturbance, were they of any serious significance.

Our thanks are due to the consultant staff of the Middlesex Hospital without whose coöperation this work could not have been done.

REFERENCES

Crofton, J., Foreman, H. M. (1948) *Brit. med. J.* ii, 71.
McDermott, W. (1947) *Amer. J. Med.* 2, 491.
Murray, R., Paine, T. F., Finland, M. (1947) *New Engl. J. Med.* 236, 701.
Selbie, F. R., Simon, R. D., McIntosh, J. (1945) *J. Path. Bact.* 57, 47.
Warner, P. T. J. C. P. (1948) M.D. thesis, University of London.

EXPERIMENTAL OBSERVATIONS ON RENAL BLOOD-FLOW

D. A. K. BLACK
M.D., B.Sc. St. And., M.R.C.P.
LECTURER IN MEDICINE

M. G. SAUNDERS
M.B., M.Sc. Manc.
LECTURER IN EXPERIMENTAL PHYSIOLOGY

UNIVERSITY OF MANCHESTER

Trueta et al. (1947) have shown, anatomically, that the kidneys of several mammalian species possess an alternative circulation in which the blood perfuses deep glomeruli and medullary tubules rather than cortical glomeruli and convoluted tubules. They have also shown that in the rabbit stimulation of the sciatic nerve or the use of various vasomotor drugs may bring this "Oxford shunt," as Americans call it, into operation.

The observations which we report briefly here were made with two main objects: (1) to determine the effect of the shunt on renal function, as assessed by inulin and *p*-aminohippuric-acid (P.A.H.) clearances; and (2) to determine by functional, as opposed to anatomical, studies whether the Oxford shunt could be brought into play in a species other than the rabbit.

We have used cats and rabbits in these studies. In one series of experiments our chief object was to assess the effect of sciatic stimulation on the inulin and P.A.H. clearance without any exposure of the kidneys. Urine was collected with a bladder cannula, and the sciatic nerve was stimulated faradically in the thigh. Urine-collection periods of 10 minutes, with bladder wash-outs, were used. After the first two periods the sciatic nerve was stimulated for 10 or 20 minutes; the collection of urine continued during stimulation and for at least 20 minutes afterwards. With this technique we observed unequivocal changes in clearance in about half the rabbits studied but in a smaller proportion of cats. The rabbit results for P.A.H. clearance are shown in table I. Five of the rabbits showed a fall in P.A.H. clearance which in some cases persisted into the period after stimulation; in other cases the P.A.H. clearance returned to normal. Inulin clearances showed a fall in those animals whose P.A.H. clearances fell, but mostly the fall in inulin clearances was smaller, with the result that the ratio $C_{In}/C_{P.A.H.}$ increased. Fig. 1 shows the results in a cat in which the clearances showed a change. In general, sciatic stimulation was associated with a slight rise in systemic blood-pressure in cats, and a slight fall in rabbits.

TABLE I—P.A.H. CLEARANCE IN RABBITS (ML./MIN.)

Rabbit no.	Pre-stimulation	Stimulation	Post-stimulation
1	15·9	8·6	12·0
2	15·9	16·3	27·8
3	14·6	14·7	10·3
4	21·9	22·5	34·8
5	13·6	14·6	15·1
6	23·7	1·4	0·2
7	16·2	15·2	17·0
8	23·6	3·5	..
9	16·1	12·6	16·1
10	14·9	4·1	0·5

Each value given is the average of two 10-min. periods. For the group of rabbits 1, 6, 7, 8, 9, and 10 application of the t test shows that the difference between the pre-stimulation and stimulation periods is highly significant ($P < 0.01$). In rabbits 2, 3, 4, and 5 there is no significant difference ($P = 0.9$).

This first series of experiments seemed to indicate that sciatic stimulation could produce profound changes in renal function, the rabbit being possibly more susceptible than the cat, a difference which would be quite understandable in view of the different renal physiology of the two species. It was difficult, however, to be sure that these changes were related to the Oxford shunt, since constriction of the efferent arteriole in the normal cortical circulation might produce the same kind of clearance changes. The conditions of experiment did not allow inspection of the kidneys at the actual time of stimulation, and removal of the kidneys after the clearance periods were over gave only equivocal evidence of a shunt having actually been in operation half an hour earlier.

A second series of experiments was therefore begun, in which the blood from one renal vein was diverted through a plastic tube, returning to the external jugular vein. Our preparation was modified from that of A. A. Glynn and J. D. Biggers.* Instead of cannulating the renal vein directly, we cannulated the inferior vena cava and ligated it between the two renal veins (fig. 2). It was possible to measure directly the renal blood-flow with a side-tube, to collect samples of renal-vein blood, and to measure the renal-vein blood-pressure.

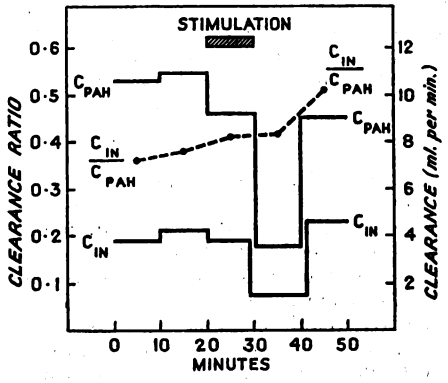


Fig. 1—Clearance results in a cat with sciatic nerve stimulated for the time shown.

The establishment of this circuit involves opening the abdomen and some interference with the renal pedicle in placing the vena-caval ligature. Rabbits stood this

* Demonstrated at Sheffield to the joint meeting of Northern Medical Sciences Colloquia in 1948.

Digitized by Google

operation badly, but we were able to observe eight cats and one rabbit in which the renal-vein outflow was 10 ml. or more per min. At this level of blood-flow defective extraction of P.A.H. from the plasma cannot be ascribed to total renal ischæmia. Normally P.A.H. is almost completely extracted from the plasma, and the P.A.H. clearance is therefore used as a measure of renal plasma-flow. Table II shows the renal blood-flow and the extraction ratio of P.A.H. $\frac{\text{(arterial P.A.H.—renal vein P.A.H.)}}{\text{arterial P.A.H.}}$ in the eight cats whose normal renal blood-flow qualified them for study. These are not normal animals, but the reduction in P.A.H. extraction by kidneys whose total blood-flow is normal is rather striking and can only mean that a substantial part of the blood flowing through the kidneys is failing to perfuse the secreting part of the tubules. This picture is sometimes induced by stimulation, but was often present with no other stimulus than the operative trauma.

An incidental observation tends to confirm the presence of an important shunt in the cat's kidney. In one animal with a narrow jugular cannula and a high renal-vein blood-flow the pressure in the side-tube was noted to be high. When outflow from the renal vein was deliberately obstructed, the renal-vein blood-pressure in most of our cats rose rapidly to 70 cm. or more of saline solution. We were never able to observe femoral or vena-caval blood-pressures in excess of 10 cm. of saline solution, even after obstruction; though failure of the blood-pressure to rise in these veins might be attributable to large venous anastomoses. In a minority of cats the renal-vein blood-pressure did not rise after obstruction. Specimens taken from the obstructed renal vein showed a poor extraction of P.A.H., and we believe that renal-vein blood-pressures of this magnitude imply large communications between renal artery and vein.

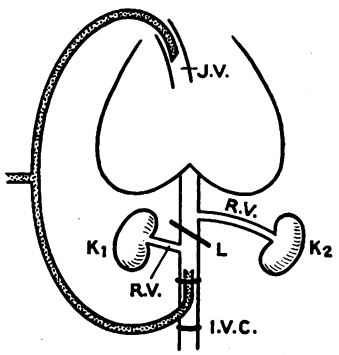


Fig. 2—Preparation used in sampling renal-vein blood: plastic tube connects renal vein (R.V.) with jugular vein (J.V.); ligature (L) ensures that blood from one kidney (K_1) passes into the tube, while the other kidney (K_2) has a normal venous drainage; I.V.C., inferior vena cava.

DISCUSSION

We have found evidence that in cats as well as in rabbits appropriate stimulation leads in some animals to profound alterations in P.A.H. and inulin clearance, which may correspond to the presence of the Oxford shunt. Moreover, in similar circumstances the extraction of P.A.H. from the blood by the kidney is impaired, even when the renal-vein blood-flow is in the normal range; and in such circumstances it is quite unreal to equate P.A.H. clearance with renal plasma-flow, though inulin clearance will continue to measure glomerular filtration-rate. The general pattern of clearances during stimulation of a type known to be capable of inducing the shunt is a lowering of inulin and P.A.H. clearance, together with a rise in the ratio of inulin to P.A.H. clearance.

Kubicek and Kottke (1946) reported a raised $C_{In}/C_{P.A.H.}$ ratio in dogs during stimulation of the renal nerves, before the Oxford shunt had been demonstrated. Theoretically, the relative changes in inulin and P.A.H. clearances will depend on the different perfusion of glomeruli and of secreting tubules respectively. The observed rise in $C_{In}/C_{P.A.H.}$ ratio will correspond to smaller impairment of filtration of inulin than of tubular excretion of P.A.H.; and might seem at first to support the view that the shunt is glomerular, through the juxtamedullary glomeruli.

TABLE II—BLOOD-FLOW FROM ONE KIDNEY AND P.A.H.-EXTRACTION RATIO IN CATS

Blood-flow (ml./min.)	P.A.H. extraction (%)	Stimulation
11	77	Sciatic
13	80	Nil
12	20	Renal-vein obstruction
20	80	Pituitary extract
20	62	Nil
10	62	Nil
10	50	Nil
12	58	Nil

Renal blood-flow was measured by direct collection, P.A.H. extraction by analysis of arterial and renal-vein blood. Stimulation "nil" means no stimulus other than operative trauma.

Some things are difficult to explain on this basis. Inulin clearance is profoundly depressed, even if not to exactly the same degree as P.A.H. clearance, pointing to a diversion of blood-flow away from the glomeruli. Moreover, the rapid increase of blood-pressure to 70 mm. or more in the renal vein is difficult to explain on the assumption that all the blood has passed through glomerular capillaries. Simkin et al. (1948) observed that glass spheres of a diameter much larger than that of the glomerular capillaries can pass through the kidneys. These things make us question the predominant rôle assigned to the juxtamedullary glomeruli in the Oxford shunt, and suggest that the medullary pathway may be largely non-glomerular.

Speculation on the part played by the Oxford shunt in conditions so diverse as crush injury and essential hypertension has far outrun any serious attempt to devise means of recognising when the shunt is in operation in man. Our observations may have some bearing on this problem. A simple fall in clearances is obviously not enough, since it could be produced by changes in vascular tone in the ordinary cortical circulation or by a fall in the systemic blood-pressure. Even when combined with a rise in filtration fraction, it would still not be definite, since either an efferent arteriole constriction or a rise in renal-vein blood-pressure (Bull 1948) could explain this pattern. Observations on the P.A.H. content of renal-vein blood, as compared with systemic blood, would be helpful, since a gross fall in P.A.H. extraction would provide real evidence that the cortical circulation was being by-passed. The only confusing factor here might be a gross reduction in total renal blood-flow from general causes leading to defective excretory function by anoxic tubules; this could be excluded by normal blood-pressure readings.

We suggest that the following criteria should be satisfied before the presence of a shunt is invoked to resolve our renal and hypertensive dilemmas: (1) low clearances of inulin and P.A.H., with some rise in the $C_{In}/C_{P.A.H.}$ ratio; (2) an extraction of P.A.H. by the kidneys of less than 80%; and (3) absence of gross changes in the general circulation.

We hope that these criteria, based on experiments on animals, may be useful to workers tackling the important clinical problems which may involve a renal shunt.

REFERENCES

Bull, G. M. (1948) *Clin. Sci.* **7**, 77.
Kubicek, W. G., Kottke, F. J. (1946) *Fed. Proc.* **5**, 58.
Simkin, B., Bergman, H. C., Silver, H., Prinzmetal, M. (1948) *Arch. intern. Med.* **81**, 115.
Trueta, J., Barclay, A. E., Franklin, K. J., Daniel, P. M., Prichard, M. M. L. (1947) Studies of the Renal Circulation. Oxford.

Digitized by Google

FATAL AIR EMBOLISM DURING BLOOD-TRANSFUSION

G. B. DOYLE M.B. N.U.I. ASSISTANT PATHOLOGIST
PATRICIA FRODSHAM B.M. Oxfd FORMER HOUSE-SURGEON
CITY HOSPITAL, NOTTINGHAM

FATAL air embolism is comparatively rare, 56 cases being reported in the decade 1932–42, of which only 4 were associated with blood-transfusion.[1] The circumstances of the case we present are most unusual and paralleled only by that of Dolton et al.[2]

On April 13, 1948, subtotal gastrectomy was performed on a man of 49 with a long-standing gastric ulcer. Some weeks previously he had had a blood-transfusion for a hæmatemesis. Clinical examination showed him to be otherwise healthy. His blood-pressure was 130/75 mm. Hg and hæmoglobin 11·8 g. per 100 ml.

On the morning of operation a saline transfusion was set up as follows: a cannula was tied into the right internal saphenous vein at the ankle with a catgut ligature, the distal portion of the vein tied off, and the skin incision sutured. A dry gauze dressing was applied, and the whole sealed off as far as possible with elastic plaster.

The apparatus used for transfusion was of the familiar type with a stockinette filter. The rubber tubing between the bottle and cannula was interrupted by a drip chamber, without a side-tube, and a glass connexion 20 cm. from the cannula. A screw clamp was applied below the drip chamber. Precautions were taken to exclude air from the tubing before inserting the cannula into the vein.

Preoperative medication consisted of 'Omnopon' gr. $^1/_3$ and scopolamine gr. $^1/_{150}$. A spinal anæsthetic of 16 ml. light 'Nupercaine' was given, and a splanchnic block performed with 100 ml. of 0·25% procaine with 1 ml. of adrenaline 1 in 1000. During the operation these were supplemented by 0·75 g. of thiopentone, 10 mg. of curare, and nitrous oxide with oxygen.

The operation (performed by Mr. E. B. Z. Masterman) lasted 2 hours 10 minutes. Five minutes after it had begun a bottle of blood (grouped and cross-matched) was substituted for the saline bottle. At the time of his return to the ward the patient was in good condition and the transfusion running satisfactorily.

The ward sister noted 50 min. later that the drip was running very slowly. She milked the tube and apparently improved the rate of flow; 10 min. later the blood-pressure was 120/80 mm. Hg, pulse-rate 100 per min., and the patient's general condition satisfactory. In another 5 min. the sister noted that the drip had stopped. She milked the tube again and shook the bottle. When the flow did not start again, she attached a Higginson syringe to the air-inlet tube of the bottle and applied pressure. The patient quickly became cyanosed, and the drip chamber was seen to be empty. The syringe was removed and the tubing clamped off. Oxygen and nikethamide were given, but the patient rapidly became pulseless and stopped breathing.

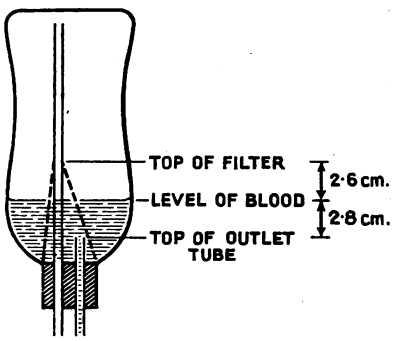
After his death it was seen that the glass connexion in the transfusion apparatus contained no blood, and crepitus was elicited in the upper part of the right internal saphenous vein but not in the left.

At necropsy the bowel anastomosis was found to be intact. All the large systemic veins of the abdomen, thorax, and neck contained air-bubbles. There was a considerable amount of air in the pelvic veins, especially on the right side. A small incision was made into the anterior part of the pericardium, and the pericardial sac was filled with water. The right ventricle was then punctured, and several large air-bubbles escaped. There was a small amount of frothy blood in the right side of the heart. The veins on the surface of the cerebrum also contained a few small air-bubbles, but this is not an unusual necropsy finding. Apart from some slight inflammation in the pelvis of the right kidney no other organic disease was noted.

DISCUSSION

Measurements of the transfusion apparatus taken afterwards showed that at the time of the accident the level of blood was 2·8 cm. above the top of the outlet tube and 5·1 cm. above the cork, and it was 2·6 cm. below the top of the filter. The ward sister could not remember clearly at what stage she shook the bottle. If she did so after applying pressure with the Higginson syringe, a possible explanation is that blood was momentarily displaced, allowing air under pressure to come in contact with the outlet tube and pass thence through the tube and cannula. We tried later experimentally to bring about such a result but could not do so at the level of the blood that we found in the bottle.

In the case reported by Dolton et al.[2] from St. Thomas's Hospital a Higginson syringe was applied to hasten a transfusion during operation, and 15 min. later the patient died suddenly, the diagnosis of air embolism being confirmed at necropsy. The relative levels of blood and outlet tube at the time of this accident are not mentioned in the report, but one assumes from the explanation given that the blood was still above the tube, as in our case. The explanation which they offer (and support experimentally by partially occluding the filter with collodion) is that the filter became partially blocked, thus slowing the drip; the rise of air-pressure in the bottle then did not hasten the passage of blood through the filter; instead, air passed through, and air and blood passed intermittently down the tube.



We could not reproduce their results using collodion; perhaps they used a metal filter. However, we were anxious to discover whether blood-clot could have a similar effect. Accordingly we brought about partial clotting in a bottle of citrated blood by the addition of calcium chloride, and ran the blood out through a similar apparatus to that used for transfusing the patient. We found that, when the bottle was a little less than half full, the level of blood being $^1/_2$ in. higher than at the time of the accident, the drip slowed down, and air-bubbles and blood entered the drip chamber intermittently. The flow soon ceased, and the level of blood in the drip chamber fell. Application of pressure then through a Higginson syringe completely emptied the drip chamber, and air passed out through the cannula.

It seems, then, that if a filter becomes partially blocked by blood-clot during transfusion the raising of the pressure inside the bottle is dangerous and may lead to fatal air embolism. How often sufficient clot is present for this to occur is impossible to say, but clots adherent to the filter are a common finding when one bottle of blood is being substituted for another. Also it must be remembered that only the part of the filter below the level of the blood need be occluded.

When donors are being bled, it is not uncommon to find blood-clots forming in the tubing when the rate of flow is abnormally slow. A bottle of blood containing some of these clots would presumably be more likely to clog a filter than one that filled at a normal rate.

PROPHYLAXIS

To prevent any similar accident it is now a rule at this hospital that Higginson syringes may be used for the above-mentioned purpose only by a doctor in an emergency. The administration sets are assembled at the regional transfusion centre to ensure the use of outlet tubes of standard length. It is probably a wise

1. Simpson, K. *Lancet*, 1942, i, 697.
2. Dolton, E. G., Gardner, E., Wylie, W. D. *Ibid*, 1945, i, 531.

Digitized by Google

precaution never to apply pressure during transfusion once the level of blood has begun to fall below the top of the filter. Macintosh and Pask [3] have designed a piece of apparatus—a glass float in the drip chamber—to prevent air embolism.

SUMMARY

A fatal case of air embolism followed the use of a Higginson syringe to expedite a blood-transfusion.

The explanation advanced is that the blocking of the lower part of the filter by blood-clot allowed air instead of blood to pass into the patient when the pressure inside the bottle was raised.

HÆMOCHROMATOSIS
IN THREE FAMILIES AND IN A WOMAN

R. D. LAWRENCE
M.A., M.D. Aberd., F.R.C.P.
PHYSICIAN IN CHARGE OF DIABETIC DEPARTMENT, KING'S COLLEGE HOSPITAL, LONDON

BRONZED diabetes is a very rare disease confined almost entirely to males, and probably due to an inborn error of iron metabolism. Sheldon's monograph [4] mentions very few familial or hereditary cases and emphasises the rarity of the disease in females. It therefore seems right to report three families in which brothers were affected and one rare female case.

FAMILIAL CASES

Family I

I have already reported [5] a family in which 2 brothers certainly, and 2 other brothers perhaps, had hæmochromatosis out of 6 males; for details the reader is referred to my previous paper.

Family II

The second family (fig. 1) consisted of the parents, 7 sons, and 1 daughter. Of the 7 sons 4 were killed in

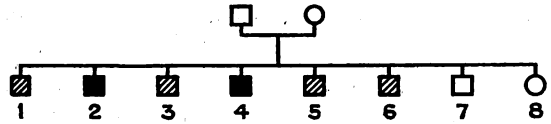


Fig. 1—Family II: square, male; circle, female; hatched, killed in 1914-18 war; black, hæmochromatosis; plain, normal.

the 1914–18 war. Neither the long-lived parents nor the daughter were diabetic.

The *eldest surviving son* came to me, because of diabetes, at the age of 52. Hepatomegaly had been discovered five years previously, a hydatid cyst had been tentatively diagnosed, and a year before he came to me the patient had undergone a Talma-Morison operation, when a typically pigmented cirrhosis had been found. Insulin 60 units daily enabled him to live a hard hunting and shooting life for three years, and then he died of ascites.

The *second surviving son* developed diabetes acutely at the age of 59, with intense wasting and ketosis. He had been known to have a very large liver for three years and, besides all the classical symptoms, had numerous darkly pigmented areas of skin carcinomatosis, particularly on the wrists and face. He did well on 50 units of insulin a day for three years, but after an attack of gastro-enteritis he died in the depths of the country from "streptococcal meningitis and diabetic coma"—the details are obscure.

Family III

This family (fig. 2) consisted of the parents and 5 sons, including a pair of identical twins so unique in their medical history that one longs in retrospect for more detail.*

The *father*, aged 72, was operated on for gall-stones in both the gall-bladder and the common duct. At 74, after a prostatic obstruction, he died with a definite severe diabetes and an enlarged liver but no splenomegaly and no pigmentation suggesting hæmochromatosis (no necropsy). The 3 brothers of the twins seem normal.

The history of the *identical twins* is better known. At the age of 28 both were diagnosed as typical cases (Harley Street standard tests) of acholuric familial jaundice and both underwent splenectomy. At 34 one twin had "jaundice," and next year he developed hepatitis with a large liver. At 36 diabetes developed and responded well to insulin. Nine months later after an attack of vomiting and cessation of insulin the man died in diabetic coma (blood-sugar 1280 mg. per 100 ml.). Necropsy sections showed every feature of hæmochromatosis.

The other twin, at the age of 36, was found, during an attack of tonsillitis, to have his liver enlarged to three finger-breadths below the costal margin. He was referred to me soon afterwards for an opinion on minor glycosuria and an abnormal glucose-tolerance test: fasting 173; after glucose 219 (½ hr.), 198 (1 hr.), 192 (2 hr.), 134 mg. per 100 ml. (3 hr.). I found typical skin pigmentation, impotence, a female type of distribution of hair, and a liver extending four finger-breadths below the costal margin but less cirrhotically hard than is usual in these cases. I diagnosed hæmochromatosis and early diabetes with confidence. He died six months later from repeated hæmorrhages from a large gastric ulcer. Widespread deposits of hæmosiderin were found in all his organs, but there was an unusual absence of hæmofuscin. This absence and the presence of iron-reacting particles in his red cells (siderocytes) suggested a disease akin to, but not identical with, hæmochromatosis (personal communication of Dr. A. H. T. Robb-Smith to Dr. Hancock).

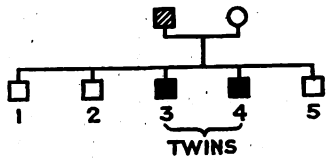


Fig. 2—Family III: hatched, diabetes without hæmochromatosis; plain, apparently normal; other symbols as in fig. 1.

Despite the atypical findings in the second twin, these twins present evidence of a genetic factor in what seemed to me typical hæmochromatosis.

HÆMOCHROMATOSIS IN A FEMALE

This disease is so rare in women that it seems worth recording the only female case I have seen, in comparison with 39 males. Sheldon [4] notes that only 16 female to 295 male cases have been published (i.e., about 1 to 20).

A woman of 66 was referred to King's College Hospital with about four weeks' history of classical symptoms of diabetes, thirst being the most troublesome. Heavy glycosuria and a blood-sugar of 384 mg. per 100 ml. were found but no ketosis, and the patient responded well to 40 units of insulin a day as an outpatient. Bronzed diabetes was suspected from her slaty-brown colour and hepatomegaly and was confirmed by skin biopsy. The rarity of the case led to the woman's admission to hospital for full investigation.

Her previous personal and family history were irrelevant. She had always been a dark brunette but had noted further darkening for two or three years. The exposed parts, face and hands, were darkest and very slaty, and the abdominal parietes browner, with some almost black spots. The mucosæ were not pigmented. The liver extended three finger-breadths below the costal margin and was hard and slightly rough but not tender; the spleen was just palpable. Axillary hair was absent, and the pubic hair was scanty and fine. The diabetes responded readily to insulin; but, as is usual in such cases, the patient regained little weight. The usual mild hypochromic anæmia was present. The erythrocyte-sedimentation rate was 18 mm. in 1 hr.

Before she died of asthenia and heart-failure three years later, this patient became as dark as a southern Indian—darker than any male case I have seen. Adrenal insufficiency was suspected from her asthenia and low blood-pressure (90/70 mm. Hg) but disproved by blood chemical tests. Necropsy showed typical deposits of iron in all the organs examined, substantiating the clinical diagnosis of hæmochromatosis.

3. Macintosh, R. R., Pask, E. A. *Ibid*, 1941, ii, 10.
4. Sheldon, J. H. Hæmochromatosis. London, 1935.
5. Lawrence, R. D. *Lancet*, 1935, ii, 1055.

* I am greatly obliged to Dr. Thompson Hancock for putting his splendid notes at my disposal, and perhaps he will and should report fuller details instead of my brief résumé of the hereditary aspect.

Digitized by Google

Medical Societies

LIVERPOOL MEDICAL INSTITUTION AND MANCHESTER MEDICAL SOCIETY

The Lipoidoses

AT a joint meeting of the Liverpool Medical Institution and the Manchester Medical Society in Manchester on March 2, Sir HENRY COHEN delivered an address on the Lipoidoses—Clinico-Pathological Study.

Interest in the lipoidoses, he said, began nearly a century ago with the description by Addison and Gull of large, pale, "foamy" cells in vitiligoidea planum et tuberosum—the lesion now labelled xanthoma multiplex. As time passed, several diseases were described as belonging to the group of lipoidoses, their common feature being the "foamy" cell. Increasing knowledge of lipoid metabolism and more intensive histological study had helped towards a clearer understanding of these conditions, which, though superficially diverse, were shown to be different facets of a uniform process.

Excluding neutral fats, the lipoidoses revealed disturbances in the metabolism of: (1) phosphatides, of which the monoaminophosphatides, lecithin and cephalin, and the diaminophosphatide, sphingomyelin, were of major import; (2) cerebrosides, of which kerasin was significant; and (3) cholesterol, which played an important rôle in bile, vitamin-D, and sex-hormone disturbances. In disease, excess of lipoid might appear in the intercellular spaces or within the cell. Extracellular lipoid deposits were seen in such degenerative changes as lipoid proteinosis and necrobiosis lipoidica diabeticorum.

Accumulation of lipoid within the cell could arise (*a*) from hyperlipæmia, the excess lipoid being taken up by cells of the reticulo-endothelial system; (*b*) from abnormal cellular metabolism leading to excessive production of lipoid within the cell; or (*c*) from both factors. In disease it would seem that one of the lipoids was primarily involved though the others were in lesser degree also affected. Thus phosphatide metabolism was disturbed in Niemann-Pick disease, Tay-Sachs disease and other forms of cerebromacular degeneration, gargoylism, and the Bürger-Grütz syndrome; while in Gaucher's disease kerasin appeared the predominant cellular lipoid.

The xanthomatoses associated with disturbance of cholesterol metabolism fell into three groups. The first appeared to be the direct outcome of a hyperlipæmia, and disappeared when its cause was removed; this group included familial types and those associated with diabetes mellitus, hepatic inadequacy, glycogen storage disease, lipoid nephroses of all types, and myxœdema. In this group was often found extensive and diffuse cutaneous xanthomatosis of neck, back, and palms and soles. The second group comprised xanthoma palpebrarum, xanthoma tuberosum et planum, xanthoma tendinosum, xanthoma of blood-vessels and endocardium (often responsible for familial and hereditary forms of coronary occlusion), and xanthomatous biliary cirrhosis. These, though associated with hypercholesterolæmia, showed evidence of intrinsic cellular dysfunction; they were not separate diseases, and all described types might be found in the same patient; they showed no significant reversibility when lipoids were withheld. Clinical evidence suggested that this form of xanthomatosis might be a precursor of calcinosis cutis of the Thibierge-Weissenbach type. In the third group were included xanthoma disseminatum, Hand-Schüller-Christian syndrome, Letterer-Siwe syndrome, and eosinophilic granuloma of bone. In these the blood cholesterol was normal. The pathological changes had a common pattern; all variations and gradations of change occurred, depending on the sites of the lesions and whether the predominant cell was the primary histiocyte, or its acidophil or "foam" cell modification.

". . . There is, to put it quite dispassionately, a definite cash value in good health and a very heavy cost in illness. . . . Economists have demonstrated that sickness costs the nation some 7% of its total annual income, and that expenditure on the prevention of disease is only 4½% of the cost of sickness."—Dr. C. SEELEY in a Chadwick public lecture on Dec. 2, 1948.

Reviews of Books

An Atlas of Traumatic Surgery

JOSEP TRUETA, M.D. Barcelona, D.SC. (Hon.) Oxfd, F.R.C.S. (Hon.) Canada, surgeon to the Wingfield-Morris Orthopædic Hospital, Oxford. Oxford: Blackwell Scientific Publications. 1949. Pp. 150. 30*s*.

THIS book was written to provide by photograph and short description a record of the methods and results of wound treatment in the latter half of the second world war. It will remain a standard and a guide to the methods and results then achieved. Wars are fought by new generations, and many of the methods of wound treatment learned by bitter and costly experience in the first world war had to be relearned by a new generation of surgeons in the second. It has been Mr. Trueta's aim to provide a record for surgeons yet to be, though we hope they never have to use it. His atlas has been well put together, with a brief description of the surgery undertaken at each stage. Photographs taken at each major stage have been beautifully reproduced, and the book is as a whole a credit to the publishers.

Scientists and Amateurs

A History of the Royal Society. DOROTHY STIMSON, PH.D. London: Sigma Books. 1949. Pp. 262. 15*s*.

THE history of the Royal Society has been written already by several authors, notably Birch and Thomas Sprat, and especially by C. R. Weld in his great work. These, however, have been concerned only with certain periods of its life and activities. Miss Stimson's book seems to be the first important account of the society from its inception up to the present time. The Royal Society first arose as early as 1645, as a practical protest against the despotism of the theories of Aristotle and Galen, still regarded, then, as the final authority on science. Its members proposed rather to follow the experimental teaching of Vesalius and Copernicus, and were thus the first exponents of modern scientific method: from the beginning their tradition was the furtherance of natural knowledge by experiment and observation. The society survived the troublous Cromwellian period, and in 1660, after the Restoration, it received at least the titular support of its official founder, Charles II. He was interested and free with advice, but he contributed little else. In its early days the membership roll showed few real scientists, but many enthusiastic literary scholars whose assistance ought not to be underestimated. Lack of financial aid nearly wrecked the society; but it survived this and also the sneers of men so distinguished as Shadwell, Samuel Butler, Addison, and even Swift. It was not until the beginning of the 19th century that the great work of the society gained the recognition it deserved; since then it has been the accepted authority in all the sciences. It is a great story, well told.

Wuchsstoffe und Antiwuchsstoffe

Ein Beitrag zum Stoffwechsel der Mikroorganismen. Dr. W. RUDOLPH. Berne: Huber. 1948. Pp. 108. Sw. fr. 8.50.

THIS little book is a product of the day. It could not have been written a few years ago, for there was not the knowledge to fill it; and the subject is now advancing so rapidly that it will soon be quite impossible to compress it into a book of this size. As the subtitle implies, the greater part of the work is devoted to the effects of these growth-promoters and inhibitors on bacterial metabolism, but their importance in mammalian physiology is also discussed. The number of these substances which have been described is already legion; Dr. Rudolph mentions, for example, 11 variants of biotin and 9 of its classical antagonist, avidin. He opens with a section on the antagonism between *p*-aminobenzoic acid and sulphonamides, and then in turn deals with nicotinic acid, pantothenic acid, the "pyridoxine" group of compounds, biotin, thiamine, lactoflavine, inositol, choline, the K vitamins, cholesterol, the purines, and finally the amino-acids. "Antivitamins" of the phytic-acid type, which were included in their discussion of the subject by the Nutrition Society, find no place in this hierarchy. With so many compounds to describe, the author has naturally

Digitized by Google

not been able to devote a great deal of space to each, but he has found room for plenty of structural formulæ which readers will appreciate. In short, he has made the most of an opportunity, and the book may be recommended. The 543 references should be enough to satisfy even the most prodigious thirst for further knowledge.

Marriage Crisis

DAVID R. MACE. London: Delisle. 1949. Pp. 141. 5*s*.

THIS book, by Mr. David Mace, PH.D., secretary of the Marriage Guidance Council, belongs to a series designed to provide accurate sexual guidance, and to counteract the action of "irresponsible literature." It is perhaps better fitted to this task than its predecessor *Does Sex Morality Matter?*: Dr. Mace stresses the importance of home stability as an argument for monogamy, and those who do not share his conception of the religious basis of sexual conduct are given less reason to charge him with rationalisation than in previous books. He is perhaps less than fair to the motives which underlie much premarital intercourse, and the problem has greater complexity than this book suggests; but in general he combines understanding with a deep desire to help the perplexed. The style of the book does not, however, strike the right key to inspire confidence in the reader. At present the prestige of science is high, while that of traditional morality is low; and much of the effect of educative literature depends on rightness of key. Lightness of touch, which the book undoubtedly possesses, is not a substitute.

Trichomonas Vaginalis and Trichomoniasis

RAY E. TRUSSELL, M.D., associate in hygiene and preventive medicine, State University of Iowa. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 277. 30*s*.

THIS must surely be the most exhaustive work ever published on so small a subject as the *Trichomonas vaginalis*. In a good and well-illustrated section Dr. Trussell covers the history and the exact morphology of the parasite, going on to describe its growth requirements and the various culture media most suitable to it. The second part of the book, dealing with the trichomonas infections in gynæcology, should help and interest clinicians. Surveying the methods of infection and reinfection of the various forms of trichomonas, the author believes that a specific organism infects the vagina and others the mouth and lower bowel. He regards cross-infection of these various sites as unlikely. In a section on treatment he examines all the usual and many unusual agents that have been employed against the trichomonas, pointing out some of the effects and dangers of the various drugs. Though it does not propound any new theories, gynæcologists, venereologists, and dermatologists will be interested in this specialist book.

Ways to Better Hearing

LOWELL BRENTANO, with an introduction by A. G. WELLS, F.R.C.S. London: Allen & Unwin. 1949. Pp. 212. 10*s*. 6*d*.

THE author of this book has defective hearing, and has therefore learned from experience how little the difficulties of the deaf are appreciated by the world at large, and how meagre is the guidance offered by the medical profession to those who have to adjust themselves to gradual loss of hearing for normal speech and perhaps eventually to the loneliness of perpetual silence. It is a manly book, inspired by hopefulness, sympathy, and common sense, without a trace of sentimentality or conscious uplift. Since it is designed for the lay reader, scientific detail is occasionally sacrificed to simplicity; but it should be read not only by those with impaired hearing but by the doctors whose duty it is to advise them. It gives up-to-date information about audiometer tests, the choice and maintenance of hearing-aids, the value of lip-reading lessons, and the folly of consulting quacks. Among the best chapters are those which discuss the education of hearing (or rather the faculty of auditory attention) and the improvement of speech. The book ends with five appendices, all written by experts in their own fields, on speech suggestions for the hard-of-hearing, psychological aspects of deafness, hearing-aid dealers approved by the National Institute of the Deaf, methods of rating the performance of hearing-aids, and instructions on how to conduct a test in one's own home when choosing the hearing-aid best suited to one's individual disability.

Die Überlastungsschäden des Skelettsystems

Dr. Med. HANS WERTHMANN. Berne: Huber. 1948. Pp. 46. Sw. fr. 8.50.

IN this little monograph Dr. Werthmann groups together under the general title of stress lesions of the skeleton a rather heterogeneous assortment of bony disorders—not only the well-known fatigue fractures of bone but also such examples of avascular necrosis as occur in the carpal lunate and the head of the femur. Osteochondritis dissecans and even slipping of the upper femoral epiphysis are also included. The result of this catholic approach is that ætiology and pathology are not as clearly set out as they might be. A number of the radiographic reproductions are rather vague, and unfortunately serial radiographs purporting to illustrate the evolution of a consolidating lesion are of different densities. On the other hand such oddities as stress lesions in os calcis and great trochanter recorded here are well worth noting, since they may be of importance in the differential diagnosis of tuberculous disease in these sites.

Cum Notitia (Bristol: John Wright & Sons. 1949. Pp. 395. 12*s*. 6*d*.).—These reminiscences of the late Dr. D. A. Alexander were apparently addressed to his son. They give the impression, at first, of random jottings of professional experiences of interest; but closer examination reveals many wise and original sayings, the product of a keen and observant mind, warning in many cases against superficial, and at times against over-subtle, diagnosis. The author frankly confesses his own failures as well as his successes. The book ranges widely over present medical knowledge and his conclusions have been shrewdly drawn after analysis of the symptoms, often conflicting, of some of his examples. Perhaps the most illuminating letters are those concerned with tuberculosis in its protean aspects. The book is written in an easy fireside manner which makes pleasant reading.

Practical Orthoptics in the Treatment of Squint (3rd ed. London: H. K. Lewis. 1949. Pp. 271. 35*s*.).—This book, by Mr. T. Keith Lyle, F.R.C.S., and Miss Sylvia Jackson, S.R.N., has been enlarged and much of it has been rewritten. It is now a comprehensive work on the modern practice of orthoptics—so full indeed that it might well have been condensed in places. Mr. Lyle does not allow his enthusiasm to lead him into false claims; but a short chapter on what orthoptics *cannot* do would have been appreciated. Most doctors overestimate the effect of this treatment, and they need to be told emphatically that the method, though invaluable in diagnosis, is rarely curative by itself. Much expensive time is wasted, up and down the country, in giving orthoptic treatment to children and adults who cannot benefit by it. This book, however, is clear and sound.

A Textbook of Pathology, General and Special (5th ed. London: Heinemann Medical Books. 1948. 2 vols. Pp. 1582. £8 8*s*.).—In their standard work, Prof. J. Martin Beattie and Dr. W. E. Carnegie Dickson, with their collaborator Prof. A. Murray Drennan, follow the classical divisions of their subject into general and special pathology; and the two volumes are a mine of detailed information. The general section gives plenty of space to modern theories, but also quotes the great pioneer works of the past; the section on inflammation is particularly good. The chapters on special pathology are more patchy, though that on the nervous system must be one of the best ever written. The section on blood also deserves high praise. Some of the other sections are rather sketchy: carcinoma of the thyroid is dismissed in 8 lines, and the female generative organs get only 18 pages, while the annotation of diagrams is sometimes misleading. Helminthology and immunology, which are adequately covered by special books, might well have been omitted, leaving more space for special pathology. Illustrations are numerous and good—and related to the text, moreover.

Digitized by Google

THE LANCET

LONDON: SATURDAY, APRIL 30, 1949

Ulcerative Colitis

THE fact that emotional disturbances can produce pathological changes in the colon is now acknowledged. The nervous pathways through which these changes are initiated are probably mainly parasympathetic from the hypothalamus. The motor parasympathetic supply of the small intestine and the proximal part of the colon, up to and including the ascending limb of the splenic flexure, is from the vagus, while the rest of the colon and the rectum are supplied by the sacropelvic nerve. PORTER [1] points out that in many cases of ulcerative colitis, and especially early ones, the disease remains localised in the section supplied by the sacropelvic nerve; this may be due either to the transmission of more impulses along this nerve or to particular susceptibility of this part of the bowel. One result of parasympathetic stimulation is hypermotility of the small intestine, such as has been sometimes observed by radiologists in patients with ulcerative colitis. This hypermotility causes an increased amount of small-bowel contents to be passed into the colon, together probably with an excess of pancreatic enzymes, which are present in high concentration in the lower end of the ileum.

PORTER believes that these enzymes may be responsible for ulceration, partly because gut as seen through a proctoscope resembles the excoriated skin around a fresh ileostomy, and partly because vagotomy has led to improvement in cases where the disease affects only the area below the vagal supply; but so far there is no evidence of any increase in the trypsin content of the fæces. Another possibility is that the bowel wall has a decreased resistance to the enzymes. Normally protection is afforded by the complex carbohydrate, mucin, which is hydrolysed by lysozyme, an enzyme normally present in the intestinal tract as well as in gastric juice, tears, and nasal mucus; and with ulcerative colitis lysozyme has been found in great excess.[2] Furthermore, the production of lysozyme appears to be under parasympathetic control; MEYER et al.[3] found in five patients with peptic ulcer an average fall in lysozyme titre of 44% after vagotomy. Thus parasympathetic overaction may well cause increased production of lysozyme with destruction of mucin, followed by lowered resistance of the bowel wall, this in turn leading to invasion both by tryptic enzymes and by normally innocuous bacteria. GRACE et al.[4] have confirmed that in ulcerative colitis the concentration of lysozyme in the stools is high, and they also discovered that the concentration varied with the activity of the disease; during a remission it was relatively low, while during relapses it rose sharply, the increase sometimes preceding exacerbation of diarrhœa. Moreover, the lysozyme concentration was definitely related to the emotional state, being low when the patient was calm and relaxed, and rising in response to stimuli such as unexpressed anger, hostility, and resentment. By contrast, emotional stimulation of normal subjects and patients with mild types of diarrhœa without ulceration caused only slight and transitory rise in lysozyme concentration. That ulceration per se does not account for the increase in lysozyme was shown by the low concentration found in a patient with ulceration secondary to carcinoma of the colon.

These findings have practical applications. The damping-down of emotional stimuli with phenobarbitone, already widely practised, is freshly justified. Belladonna, or one of its alkaloids, is also often used, especially where pain is prominent; and routine use may well be advisable. To inactivate the pancreatic enzymes, PORTER uses sodium alkyl or lauryl sulphate (both sulphonated fatty alcohols), and MEYER has found that these agents bind and inactivate lysozyme as well; they are best given in enteric-coated pills in doses of 100–200 mg. three times a day. Sulphonamides or other antibiotics seem seldom to have much effect on the course of the disease, but a short course of one of them to combat secondary infection of the damaged mucosa seems rational, especially in the more acute type of case. Apart from these drugs, the full medical régime must include a low-residue, high-calorie, high-protein diet with added vitamins and iron. Blood-transfusion may be necessary to maintain the hæmoglobin level, and liver injections two or three times weekly are sometimes recommended. The psychiatrist's help may be sought when the condition is under control; but PORTER believes that premature psychiatric investigation may actually aggravate the bowel lesion.

Failure of medical treatment raises the question of ileostomy, which may sometimes be followed by colectomy. Ileostomy is indicated first in the acute fulminating type of the disease, where it is done as a last resort and is seldom successful, and secondly in the chronic type where the illness has pursued a relentless course for several years, with little or no remission or with persistent relapses. These patients are leading miserable lives, unable to work or enjoy social activities; depression and frustration add to the discomforts of their disease. To them ileostomy offers the possibility of return to an almost normal life; but, as MCKITTRICK and MOORE,[5] of Boston, observe, they should in fact have experienced this miserable exis-

1. Porter, S. A. *J. Amer. med. Ass.* 1949, **139**, 208.
2. Meyer, K., Gellhorne, A., Prudden, J. F., Lehman, W. L., Steinberg, A. *Proc. Soc. exp. Biol., N.Y.* 1947, **65**, 221.
3. Meyer, K., Prudden, J. F., Lehman, W. L., Steinberg, A. *Ibid*, p. 220.
4. Grace, W. J., Seton, P. H., Wolf, S., Wolff, H. G. *Amer. J. med. Sci.* 1949, **217**, 241.
5. McKittrick, L. S., Moore, F. D. *J. Amer. med. Ass.* 1949, **139** 201.

Digitized by Google

tence before operation is undertaken, for only thus will they know that the benefits of ileostomy outweigh its inconveniences. McKittrick and Moore followed up 110 patients who left hospital with an ileostomy. Of these, 6 had died from other diseases. Of the remaining 104, 88 (84%) reported that they were in good health. Maladjustment was commonest in men of poor intelligence who found difficulty in looking after the ileostomy while engaged in outdoor work, and in young unmarried women who could not endure the thought of marriage with such a disability. To the majority, however, this operation brings a new lease of life.

Care of the Old

Many an optimistic body—voluntary or municipal—has opened a home for elderly persons without considering what it means to take full responsibility for them until their death. It has never been easy—and it was always unwise and unnecessary—to remove the elderly to hospital for minor diseases, and we are glad to know that the Ministry of Health encourages all homes and hostels for the aged to set apart one room as a sick-bay. The London County Council, for example, have lately announced plans, in their homes, for "the accommodation and nursing of residents during illnesses which are ordinarily nursed at home." This intention should not be hard to fulfil, though it seems possible that sick-bays will sometimes be used for illness more serious than was intended. Unhappily the L.C.C.'s further plans "for enabling residents to obtain the benefit of any of the services provided under the National Health Service Act of which they may from time to time be in need" cannot imply that arrangements will always be made to get these elderly patients admitted to hospital when they become ill with any disease that may render them bedfast. We all well know the difficulty of securing admission for such people.

Part of this difficulty arises from the belief that elderly patients with chronic diseases cannot be restored to ordinary activity, or even benefited. The fact that beds in the former poor-law hospitals are blocked for years by these unfortunates makes every institution reluctant to add to their numbers by fresh admissions. Yet the work of Dr. Marjory Warren, Dr. L. Cosin, Dr. Trevor Howell, and others has shown that long-term illness is neither inevitable nor irremediable in the elderly. These workers have proved that something like half the patients admitted to chronic wards can be improved to such a degree that they no longer need skilled nursing and medical care. In other words, given the right treatment, the patients cease to need a hospital bed. But, as things stand at present, very few of them receive the right treatment, largely because very few doctors are trained, or in training, to provide it. Another obstacle in the way of increasing the turnover of beds is that, only too often, once an elderly patient has got into hospital, he ceases to have any other refuge. The home of the solitary old person commonly has to be given up when he falls sick; and even when there are other members left in the family it may be so manifestly unsuitable that the patient cannot be sent back to it. Obviously we should be able to transfer these improved patients to residential homes where they could live a more normal life and from which they could easily return to hospital if need be. Our aim should be to use hospital beds so far as possible for purposes of investigation and treatment, and expedite movement through them. This does not mean the aged should be excluded: as Prof. A. P. Thomson pointed out in his Lumleian lectures,[1] the danger of blocking acute beds with long-term cases can be overcome if old patients are properly classified. They should have a chance of being investigated in a general hospital. Some will need only a short course of treatment before being sent back to their residential homes, or to their families. Others can be transferred after investigation, to an institution where they can be given prolonged care. Till all this is done we shall remain very short of beds, and we ought therefore to make full use of the alternative method of bringing the hospital service to the patient. At St. Helier Hospital, Carshalton, if admission of an old person has to be refused, a social worker visits the patient's home and reports her findings to the medical staff, who can then, after consultation with the patient's own doctor, arrange whatever medical and social services will help in the management of the illness. These may include provision of nursing equipment, special bedding, "meals on wheels," investigation by X rays or laboratory, physiotherapy at home, or transport to the outpatient department for physiotherapy. This may not be as satisfactory as admission to hospital, even for a short while; but it enables many elderly patients to receive some of the main advantages of hospital care—comfort, good food, investigation, and special treatment.

The plight of old people is one of the biggest and most embarrassing problems facing the National Health Service. The poor-law, it is true, did not offer an efficient medical service for those in its care; but one of the ironies of its abolition is that the easy transfer of elderly patients from institution to infirmary and back again has been abolished, and that no corresponding system has been arranged to take its place. The National Health Service is responsible for the care of the sick, while National Assistance and the local authorities are responsible for the care of the healthy; but in old age there is no clear dividing line between the healthy and sick. Among the old, too, there are large numbers neither healthy nor sick, but infirm. To whom do they belong? To the regional hospital board or the local authority? Will the regional hospital board be able to establish, and take responsibility for, homes for them? In an article which we publish this week Dr. C. A. Boucher proposes that the boards and the local authorities should jointly appoint "physicians for the elderly" whose task it would be to mobilise the different kinds of resources needed for the proper care of the old. These doctors, he rightly feels, should not be strictly specialist in outlook or qualifications: the illness of the elderly should not be separated by a rigid bulkhead from the illness found in middle age or even youth. A medical service such as Dr. Boucher recommends should aim at restoring as many as possible to a state where they can lead independent or semi-independent lives. This is what the old people

1. *See Lancet*, April 16, p. 657.

Digitized by Google

themselves want. Moreover, it gives those who wish it the chance to contribute, according to their power, to the country's wealth. They enjoy simple outwork and it does them good. An interest in life is the best defence against senility.

Virus and Cancer Cell

THE latest report from the Imperial Cancer Research Fund[1] is of absorbing interest to all engaged in studying cancer research: it "deals chiefly with a long-continued, difficult, uncertain, and finally successful research on the propagation of tumours of mice with dry tumour tissue" whose results were outlined by Prof. W. E. GYE, F.R.S., the director, in a lecture at the Royal College of Surgeons on March 22.[2] Writing with his accustomed grace, GYE draws on the discoveries of half a century's investigation; the epigrams of past leaders are blended with an unshakable faith in the virus theory of cancer and with courageous expeditions into the darkness that conceals the secrets of malignancy. Sometimes he seems to be giving a fencing display against the opponents of his beloved theory; sometimes he appears as the triumphant captain who, after a dangerous voyage, has brought his ship safely home at last. Critics have wasted no time in pointing to the gaping holes in the craft's structure; they say that his proof depends on still unproven data. But undoubtedly the evidence for a virus as the agent in the Shope rabbit papilloma and as the Bittner factor has given powerful support to his position; moreover the continual repetition of the terms "plasmagene" and "cytogene" at discussions of cancer theory indicates that opinion has inclined still further in the viral direction.

GYE propounds that, though mammalian cancers may be initiated by chemical or physical means, the continuing cause is a virus. And, after all, there is nothing difficult (except the proof) in the idea that mammalian as well as avian tumours are transmitted by units of subcellular dimensions; for such units are becoming increasingly prominent in biology—e.g., the cellular and nuclear organelles and other components, the microsomes, and other lipoprotein complexes of some degree of stability. He suggests that the virus is present in a latent form in all tissues; when, for instance, a mouse is injected with methylcholanthrene, the damaged cells permit the entry of the virus, which proliferates, brings about malignancy, and is then in an active form. The difficulty of explaining why mammalian tumours (with the two exceptions mentioned) have not previously been transmitted by subcellular agents could be overcome by a number of suppositions; for example, that the agents are unstable when separated from the protective constituents of the cell. An analogy can easily be found in the fact that rat liver slices can synthesise cholesterol but that liver mash can no longer do so. As evidence of local infection of non-malignant tissue by virus, GYE puts forward the sarcomatous transformation of mouse mammary carcinoma.

1. Forty-sixth Annual Report of the Imperial Cancer Research Fund, 1948–49. Presented at the annual general meeting on April 20. Obtainable from the fund's office at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2.
2. Published in the *British Medical Journal*, March 26, p. 511; summarised in *The Lancet*, March 26, p. 535.

The second part of the evidence for the infective theory of tumour induction forms the main part of the report: it lies in the discovery by GYE and his collaborators that mouse sarcoma is transplantable after freezing and drying. It has long been known, and has often been demonstrated, that mere freezing of mouse tumours does not impair the capacity for successful grafting; but the transplantability has usually been attributed to the survival of cancer cells. GYE, on the contrary, believes that the cold kills the cells, and that grafting depends on the unaffected virus component of the tumour; its resistance to drying (resembling the resistance of other viruses) adds to the certainty that the tumour cells are indeed destroyed by the two processes. To this the critics simply reply that freezing does *not* kill the cells, and that the method used by GYE does not dry them. And he himself does not seem wholly happy on this question of freeze-killing; for honesty has made him express himself with ambiguity and tautology. Thus, he writes:

> "It is very difficult to believe that delicate mammalian cells can withstand such low temperatures for so long and survive."
>
> "Judging by our own experience, which is supported by the few reports available of similar kinds of work, we should expect that very finely minced tissue would be less able to survive freezing if activity of frozen material depends solely on cell survival."
>
> ". . . it seems likely that not a single tumour cell survives freezing for months or even weeks and it is therefore impossible to conclude that the activity of frozen tissue is dependent on surviving cells."
>
> "Similarly, the fact that freezing suspensions of tumour cells for a few hours at −79°C kills all or nearly all the cells is revealed by serial sections of early stages of grafts. . . ."
>
> "When this kind of experiment is repeated with malignant tissue—mincing the tissue with scissors or a mincing machine, subjecting the mince to a temperature of −79°C for 3 hours, inoculating the tissue into mice and then examining the graft at intervals from 2 to 7 days—it is difficult to find a normal cell. Occasionally it is possible to detect one and from this a daughter tumour may arise."
>
> "If, as is almost certain, low temperatures kill the delicate mammalian cells but do not affect the virus, which is what might be supposed on our present knowledge of cells and viruses. . . ."

But what are the criteria of cell death? Has the dead tumour been cultivated in vitro? (Unfortunately in-vitro culture is a more severe test of viability than in-vivo propagation.) Have the respiration and other metabolic processes of the frozen tissue been sufficiently studied? Can the new virus be filtered and centrifuged? What proof is there that the tumour tissue was completely dried? These are some of the questions which must have occurred to cancer workers since the publication of Professor GYE's report. Needless to say, confirmation of his results would create a much more satisfactory state of affairs than non-confirmation, for in that case he could always refer to an unfavourable condition of the tumour virus (well known to occur with the Rouse sarcoma). The weakness of his position is that he is balancing one assumption, the mammalian virus, on another assumption, the freeze-death of the cells. But of course, the history of research would be very different if nobody had succeeded in holding weak positions until they were strengthened.

Digitized by Google

Annotations

THE NAPKIN AGE

PERHAPS in a primitive society it is not very puzzling to be a mother. But in families that enjoy all the benefits of civilisation the mother is hard put to it to keep abreast of her duty. Twenty years ago she was not allowed to pick up the crying baby and pet him, and she was expected at all costs to get him clean in the first year—or preferably in the first month—of his regimented life. Now she is encouraged to pick him up the moment he cries, and to let him get clean at his leisure.

A sharp divergence of opinion was evident in the learned discussion of toilet training held by the pædiatric section of the Royal Society of Medicine on April 22. Some held, with nice scientific detachment, that the mother should put up with heavy washing-days during the first 18 months or 2 years of her little one's life, in the hope of getting a poised child later, while others thought the price of this privilege unduly high. (Women doctors and fathers of families fell into this second group.) As an anthropologist, Mr. Adam Curle, of the Institute of Human Relations, was able to relate toilet-training to general behaviour trends in various primitive societies: the belief that it is something to be taken seriously and enforced with threats and punishment seems to go with such aggressive manifestations as head-hunting and the pursuit of witchcraft; whereas an easy-going attitude is characteristic of peaceful tribes. We stand half-way between the peaceful and violent types, he thinks, though in the last 60–80 years the increase of water-closets, carpets, and linoleum, and advances in general hygiene, have possibly heightened the importance of toilet training, and no doubt of violence, among us. He spoke favourably, however, of some British country villages he has studied, where the children are regarded with interest and affection from the moment of birth, where toilet-training and regular feeding-times are pleasantly ignored, and where children are early taken into family consultation, rove at will into any house in the village, and though always well clad are never blamed for getting dirty. In defence of primitive societies he remarked that some of their practices—such as elaborate initiation ceremonies for adolescents—give the members a strong feeling of unity with the group: they are spared the sense of being deviant outcasts so common among members of our own society.

Perhaps it was this remark which provoked the asperity of Dr. Letitia Fairfield. Anthropologists, she said, are inclined to speak of primitive societies as Communists do of Russia. Life, she believes, is not only made for babies. People grow up, and there must be mutual agreement between the ages. Unless children are trained to be clean, the family lives in an atmosphere of filth and stench which lowers its whole standard of living; and those who continue throughout life to wet the bed cannot get jobs, and have a very sad time. Miss Agatha Bowley, of the Foundling Hospital training and research centre, whose approach was more academic, pointed out that habit-training is not a mere matter of conditioning: it involves the emotions. She quoted opinions to the effect that after the age of 18 months the child who is allowed to develop without training will, if provided with appropriate pots and lavatories, train himself. It is possible, of course, to condition the child to be clean in the first year, but in her view the pot should not be too much in evidence until he is a year old and has formed a steady emotional relationship with one adult. A mild approval should reward a successful result with a pot offered at the appropriate time, and a mild disapproval should greet an accident. "Placid but not premature potting" was her advice. Dr. I. Hellman reported that 70% of children conditioned to be clean in the early months relapse between 9 and 14 months, when they have to learn the process again, intellectually; and this is such a disappointment to their mothers that they cannot take the situation coolly. She finds that obstinacy, tantrums, and a far-reaching break in the mother-child relationship result; but this was not the experience of Dr. Lindsey Batten, who always warns mothers about this relapse, and finds that most of them take it with philosophy and humour. He noted, too, that when the child goes on to a mixed diet its urine becomes irritating, and if it is still wet its genitalia and thighs get sore. "If it can, without psychological damage, be persuaded to be a bit drier than that, surely it would be an advantage?" Dr. Portia Holman, while agreeing that it might be as well to postpone training until the child had some cerebral control, felt it was not enough to say "let the mother put up with the washing." Nothing is so dispiriting as festoons of washing all over a small working-class house; it could surely be done, she suggested, on a communal basis.

Dr. Richard Asher, who owned to having three children under 5, some wet some dry, thinks there is some evidence that children who are conditioned early to be clean fail to get cortical control until later than they should; but the meeting was saved from despair by the timely recollection of Prof. J. M. Smellie, who presided, that there is such a thing as the gastrocolic reflex. Mothers can take advantage of this benign device during the first 12 months, and so, without inflicting trauma, avoid excessive washing.

LEPTOSPIROSIS IN DENMARK

WHEN he addressed the Royal Society of Medicine on April 13, Dr. C. Borg Petersen, of the State Serum Institute, Copenhagen, recalled that in Denmark very few cases of Weil's disease were recognised up till 1934, when Miss M. Zuelzer showed that in that country, as in others, a high proportion of rats are carriers of *Leptospira icterohæmorrhagiæ*. During the next six months 14 cases were brought to light, and thereupon the State Serum Institute, which is responsible for all the laboratory diagnosis of human disease in Denmark, undertook to carry out examinations for leptospirosis.

In a number of cases, the clinical diagnosis of Weil's disease was confirmed by serological methods, but the records showed that most of the patients had suffered from jaundice. Experience in other countries suggested, however, that jaundice was absent in about half of the cases; so it was decided that all sera sent for Widal tests should also be examined for the presence of leptospiral agglutinins. As a result, many anicteric cases of Weil's disease, and also some of canicola fever, were identified.

In 1937 strains of a new serological type, *L. sejroe*, were isolated from several patients, and later from harvest mice (*Mus spicilegus*), to which attention had been directed by epidemiological evidence. Qualitative receptor analysis showed this leptospira to differ from known species; but another type, *L. saxkoebing*, closely related serologically and also infective to man, was found to be carried by wood mice (*Apodemus sylvaticus*) and by harvest mice. There is no clinical difference between these two forms of leptospirosis, and if the strain of leptospira is not isolated from the patient, and if only serum is available for investigation, it is not always possible to determine with certainty the causative type by serological tests. In his epidemiological work Dr. Petersen has considered these two infections together as leptospirosis sejroe because he believes that they belong to a single serological group Further experience may show that this group contains other members, but it is sharply separated antigenically from the leptospiræ of Weil's disease, canicola fever, and mud fever. These infections occur almost entirely in rural areas. The incidence of cases in man rises steeply in summer

Digitized by Google

and autumn, but the attack-rate shows an interesting difference between the two sexes. The number of cases among males increases rapidly during harvesting, which in Denmark is carried out mainly by men. In females, infection usually occurs later, when the crops have been carried in and the mice have followed them to the farms. During 1943 a plague of harvest mice was associated with an unusually large number of human infections, about 150 cases being diagnosed during that year.

Some of the other forms of leptospirosis are also seen in Denmark, but only in small numbers. A few infections with *L. grippotyphosa* have been identified, all in males living in the rural districts of South Jutland; this is the only part of the country where the carrier host, *Microtus arvalus*, exists. *L. bataviæ* is also found occasionally in man, but has not yet been isolated from local mice. Another serological type, *L. ballum*, is present in mice; so far it has not been recognised in cases of human disease in Denmark, though one laboratory infection has recently been reported from Holland.

METOPON

FOR clinical evaluation, methyldihydromorphinone ('Metopon') was made available to doctors in the U.S.A. for thirteen months in 1947–48, under the supervision of the committee on drug addiction of the National Research Council. All the patients receiving the drug were terminal cancer cases, and most had had previous medication with narcotics. The drug was given by mouth, and nearly always the dose was between 3 mg. and 9 mg.

An analysis[1] of 3672 reports reveals that the side-effects of metopon are less than those of morphine: the commonest are nausea and vomiting, while agitation and sweating sometimes occurred; but in 82·4% of cases there were no side-effects at all. As an analgesic it seems to be at least as effective as morphine; and it is effective without dulling the mind. With terminal cancer this is not necessarily an advantage, but it certainly would be on occasions—as after operation—when the pain, though severe enough to require an opiate, is unlikely to last long and the patient's mind is best kept clear. On the other hand, the sedative action is less than that of morphine; in some 75% of cases there was no sleep that could be attributed to its effect. Tolerance develops more slowly than to morphine; but the figures demonstrate cross-tolerance between metopon and other narcotics. The drug is most valuable where morphine derivatives have not previously been used.

The report brings to light very little information about addiction; but since metopon has comparatively little effect on mental alertness and does not satisfy established dependence upon another drug, addiction probably develops less rapidly than with morphine.

THE INTERNATIONAL CLASSIFICATION

THE new classification of diseases and causes of death[2] is a work that merits the attention of all members of the profession, and is likely to become the standard for a wide range of medical statistics. Technically it is the sixth revision of the International List of Causes of Death, but a valuable advance has been made in producing a single list suited to morbidity as well as mortality statistics. Actually volume I includes no fewer than four classifications of disease: (1) a detailed list of rather more than 900 categories, resembling the Medical Research Council's provisional classification; (2) an intermediate list of 150 causes for tabulation of morbidity and mortality by age-groups and other demographic characteristics; (3) an abbreviated list of 50 causes for tabulation of mortality in administrative subdivisions; and (4) a special list of 50 causes for tabulation of morbidity for social insurance purposes. The greater part of this volume, however, is occupied by a tabular list of diagnostic terms defining the content of each category in the detailed list. The second volume will contain an alphabetical index.

Features of the new manual are an international form of death certificate (with rules for classification of causes), a suggested form for the multiple-cause tabulation of mortality figures, and a reprint of W.H.O. regulations regarding nomenclature.

The detailed list is in seventeen main sections, dealing first with diseases caused by well-defined infections, followed by neoplasms, allergic, endocrine, metabolic, and nutritional diseases. Other diseases are arranged mainly by anatomical site, with special sections for mental diseases, complications of pregnancy and childbirth, certain diseases of early infancy, senility, and ill-defined conditions, including symptoms. Alternative classifications of injuries are provided, according to external cause or according to nature of injury. Some of the categories are broad, and the classification is of course not intended to serve the function of a nomenclature of disease; but it is applicable to a great variety of statistical purposes, and the numerical coding has evidently been devised to facilitate mechanical tabulation through the medium of punched cards. Statistics produced in accordance with this classification will gain much in value through their comparability with similar statistics published in other countries associated with the World Health Organisation.

AIR EMBOLISM DURING TRANSFUSION

DURING the war, the need to restore blood volume rapidly in cases of severe oligæmic shock led clinicians to assist the inflow of blood or plasma by raising the air-pressure in the transfusion bottle, for which purpose they used a Higginson's syringe attached to the air-inlet tube. The practice thus introduced has been continued; but it is definitely dangerous unless the transfusion is closely and constantly watched while the air-pressure is being raised. In our present issue Dr. Doyle and Dr. Frodsham repeat the warning already given by Dolton et al.[1] They draw attention once more to the possibility of air embolism when the bottom part of the filter within the bottle becomes blocked or partly blocked with blood-clot, and the air under pressure takes the path of less resistance through the top of the filter exposed above the blood and thus passes through the rubber tubing into the vein. In the case they record the glass outlet-tube of the bottle apparently projected some 2·3 cm. above the rubber bung; so, if this filter had not become blocked by clot, air would have been pumped into the vein while the level of the blood was still about an inch above the rubber bung.

The lesson to be learnt from these accidents is that raising the air-pressure within the transfusion bottle is legitimate only if undertaken with extreme care. Doyle and Frodsham's suggestion that it should only be performed by a doctor is a good one and might well be generally adopted. Similarly, the air-pressure should not be raised by using a Higginson's syringe when the level of the blood has fallen below the filter, since it is impossible to see whether the blood contains clots. Unfortunately it is difficult to ensure that blood is collected without formation of any clot. The acid-citrate-glucose anticoagulant of Loutit and Mollison,[2] now in general use, contains twice as much citrate as is theoretically necessary to prevent coagulation; but clots may

1. Eddy, N. B. *Publ. Hlth Rep., Wash.* 1949, 64, 93.
2. Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death. Geneva: World Health Organisation. 1948. London: H.M. Stationery Office. 1949. Vol. I. Pp. 376. In 2 vols. 30s.

1. Dolton, E. G., Gardner, E., Wylie, W. D. *Lancet*, 1945, i, 531.
2. Loutit, J. F., Mollison, P. L. *Brit. med. J.* 1943, ii, 744.

Digitized by Google

still form unless the blood and acid-citrate-glucose solution are shaken during collection, and it is important that particular attention should be paid to this detail of technique when donors are being bled.

PREVENTION OF SUNBURN

IN Britain sunshine is seldom a burning problem; and this perhaps explains why most of the recent work on protecting the skin against the sun's rays seems to have been done in America. A year or two ago Luckiesh and Taylor [1] suggested the application of a refined grade of petrolatum with 10% salol in yellow petrolatum *U.S.P.* Since then Shaw [2] has recommended topical application of a 5–10% solution of *p*-aminobenzoic acid in 70% alcohol, while Sulzberger and Bayer [3] have reported good results from applying the acid in 10% alcoholic solution and in oil-in-water emulsion creams; esters of *p*-aminobenzoic acid have also proved satisfactory. When alcoholic solutions are applied, the alcohol evaporates leaving a film of powder, which is rubbed into the skin. Shaw claims that by this method patients who were extremely sensitive to sunburn were able to expose themselves for 8–12 hours to intense sunshine in Florida and Mexico, without the slightest discomfort; but he observed that, while *p*-aminobenzoic acid was often effective in protecting people suffering from lupus erythematosus, it was ineffective in photosensitisation dermatitis.

A further substance now advocated as a preventive of sunburn is phenazone (antipyrin), which is said to be efficient in various vehicles and concentrations.[4] This chemical has the merit of being readily available; but when given internally it can cause skin eruptions, and with repeated applications to the skin it may perhaps produce sensitivity.

SEX EDUCATION FOR MEDICAL STUDENTS

PATIENTS often complain that, of all the problems they bring to the doctor, those arising out of sexual abnormality or sexual ignorance find the least satisfactory reception. Hostility towards such problems, and to those who bring them, remains sufficiently common among doctors to prevent the patient from discussing them with the one person who might be expected to provide informed advice. Their reluctance hampers advances in treatment, and in marriage guidance, more than the public or the profession realise. Some of the difficulty arises from the lack of public instruction, and this is being gradually remedied through the educational services. The medical student, however, still receives no systematic teaching on a highly important subject, and has to obtain his knowledge mostly by his own efforts. The field of sexual psychology has an unfortunate attraction for psychopaths, and not all the literature to which he can turn is likely to be of value to him. Confronted with a problem arising out of homosexuality in an adolescent, or a minor abnormality of sexual impulse which is threatening the stability of a marriage, the newly qualified doctor today is no better off, so far as the teaching given him is concerned, than his counterpart of 1914. Indeed, he often shares all the prejudices of his time. It is hardly surprising if he reacts badly toward the inquirer, or passes the case to an already overworked psychiatric and marriage-guidance service.

The Goodenough report on medical schools, while it refers to the need for marriage-guidance instruction and for training in normal psychology, makes no specific recommendation for coping with this problem. In many medical schools even contraception is inadequately discussed; and a certain reserve is apparent in academic boards when the subject of sex education is raised. Voluntary bodies are hardly fitted to supply the need, but the universities might well consider the provision of vacation courses by reputable and experienced lecturers. The response of the student, who is generally more fully aware of his own difficulties in this field than his teachers, is certain. It remains for the teaching bodies to see that the information he receives is adequate and correct.

1. Luckiesh, M., Taylor, A. H., Cole, H. N., Sollmann, T. *J. Amer. med. Ass.* 1946, **130**, 1. See *Lancet*, 1946, i, 577.
2. Shaw, C. *J. Tennessee med. Ass.* 1946, **39**, 329.
3. Sulzberger, M. B., Bayer, R. L. Year Book of Dermatology and Syphilology, 1946. Chicago, p. 150.
4. Quiroga, M. I., Malbrán, C. F., Mom, A. M. *Prensa méd. argent.* 1948, **35**, 2399.

GLASSES OFF THE PEG

FEW who have serious defects of vision can take without blinking the news of delay in the filling of a prescription for glasses. However careful the owner, there is always a chance that a necessary pair of spectacles will be shattered, and that reserves are out of date, lost, or inaccessible. The immediate handicap imposed can be enormous; and the airy assurance that "it will take three months," to which one of this week's peripatetic correspondents was treated, can seem like a sentence to three months inside a personal fog-bank. The man in such a case, if he has eyes that are alike, could do worse than follow our correspondent's lead. There seems to be no evidence that glasses bought from a tray, whether in Woolworth's or elsewhere, do any damage. Glasses, after all, are pieces of glass which help to focus the rays of light, and they have no effect, whether curative or harmful, on the eye which uses them. If they are correct and needed, they help the wearer to see clearly and without tiring; if they are incorrect, reading will become more tiring, but it does not follow that any harm has been done. People talk of eyestrain after reading, but they do not speak of leg-strain after walking, or stomach-strain after taking a meal. The eye may become tired; it will not be strained.

The difficulty about glasses bought from a tray is that they always give the same correction for each eye; and if the chooser needs different corrections he cannot be fitted satisfactorily. Even so, he may be able to get glasses to tide him over till his proper pair is ready, and no harm will come of it.

SUPRARENAL HORMONE IN RHEUMATOID ARTHRITIS

DEEP interest has been aroused by the *Times* report of April 23 that rheumatoid arthritis has been successfully treated at the Mayo Clinic with a hormone obtained from the suprarenal gland. Of 16 cases treated all are said to have responded favourably, and in 5 the improvement is described as "very marked." These are small numbers, and no details have yet been published; but the facts as known here make it safe to assume that a new and important therapeutic effect on this difficult disease has been demonstrated. It has long been known that the rheumatoid state is reversible, at any rate temporarily; for example, it sometimes clears up during pregnancy or an attack of jaundice. Following this clue in five years' investigation, the Mayo Clinic workers have achieved a large degree of success. The *Times* correspondent also mentions "encouraging results" in rheumatic fever, and remarks that, because the suprarenal hormone produces euphoria and increased mental capacity and activity, "there is even a hope that it will prove useful in the treatment of mental diseases, particularly melancholia and depression." For full information we may have to wait until the International Congress on Rheumatic Diseases opens on May 3 in New York. Unfortunately the substance used is difficult to prepare, and will remain scarce until the difficulties have been overcome: it has not yet been fully synthesised. Moreover, there is reason to think that, like insulin, it controls rather than cures, and that its use will therefore have to be continued by the patient.

Digitized by Google

Special Articles

A PLAN FOR THE AGED

C. A. BOUCHER
D.M. Oxfd

IF we regard as "old people" all those now entitled to a retirement pension—namely, all women over 60 and all men over 65—we find that during this century their number in the United Kingdom has increased from 2½ million to over 6 million. Their proportion has also risen in steady and relentless fashion, and it is now estimated that a seventh of our total population is of pensionable age. Statisticians consider that, despite recent improvement in the birth-rate, the position will worsen during the next twenty years, and it is evident that, unless the whole problem is wisely managed, an increasingly heavy load will be placed on the shoulders of the diminishing number of wage-earners, since they must maintain both children and old people. Crushing taxation at the expense of fewer taxpayers will entail a lower standard of living, associated with a contraction of the educational, medical, and social services. Many old people are willing and competent to work after reaching pensionable age, and this should be encouraged, not only because they would continue to contribute something to the State, but because employment would help to maintain their mental and physical health and prevent the senile deterioration so commonly seen shortly after retirement. On the other hand, continued employment of old people may of course have repercussions among their younger colleagues who naturally aspire to the highest posts.

At the birth of the National Health Service about 70,000 aged persons were being accommodated in public-assistance institutions and in local-authority homes; these people—about 1% of the total aged population, were in varying degrees of health, infirmity, and sickness. The remaining 99% were living alone or with their relatives or close friends, or in hostels, boarding-houses, and hotels—sometimes in squalor and sometimes in comfort. The plight of the old is not confined to any one class: the lot of the widow, living alone on £300 a year, may be just as harsh to her as that of the pensioner getting 26*s*. a week, and living in the surroundings to which he has always been accustomed.

GULFS AND GAPS

A narrow line divides those old people who are well and those in varying stages of ill health or infirmity, and even sickness. The former may require care and accommodation, while the latter may require medical and nursing supervision and guidance, or sometimes hospital treatment. Old people who fall ill deteriorate rapidly, yet they are often unable, because of their age, to gain admission to hospital. Doctors in general practice, because of pressure of work, cannot give them adequate attention, especially if their home conditions make satisfactory nursing impossible. Nursing-homes are congested and anyhow cater only for the few who can afford the expense. Old people take longer than their juniors to recover from the illness and are more debilitated by it; if they are in hospital, difficulty of discharge then arises. The abolition of the poor-law and the establishment of the National Health Service has created an ill-defined and wide gulf which it is almost impossible to bridge. Hospital beds become blocked, to the despair of doctors, nurses, and patients. It has been decreed that a person is either well—in which case he follows his normal existence among the healthy community—or he is ill, in which case he is admitted, if fortunate, to hospital, for skilled treatment and nursing. Those in the unhappy third group of the frail yet ambulant, who require care and supervision and medical guidance, are neglected because their needs are largely invisible. The result is that the old person, who is entitled to proper medical care, is unable to gain admission to hospital or, if he succeeds in doing so, finds it almost impossible to get discharged.

During the last few years a small group of enthusiastic medical experts, working in former local-authority hospitals, have shown that much can be done in the medical rehabilitation of the aged sick; they have shown that half these patients could be discharged, after treatment, to suitable homes and hostels if these existed. About 20% of the remainder would become bedfast in spite of all treatment, while the others during the course of the year would die. Thus active treatment, followed by discharge, would greatly alleviate the present strain on hospital beds and nursing staff, and would give hope and relief from pain and deformity to many thousands of old people who have long been neglected.

These successes, however, take skill, patience, and a long time, and require great enthusiasm—enthusiasm which is at present limited to a small group of pioneers, in spite of all that has been written on the subject during the last few years. These doctors are working in isolated hospitals and are demonstrating quite clearly what can be done by those who have experience of such cases. There is a danger, however, that their zeal and success will emphasise the clinical aspect of a problem which surely has many facets. It is believed that about a third of the old people in the country fall ill every year, and need the services of a doctor; yet only a very small proportion of those suffering from treatable conditions ever reach hospital; the pure hospital clinician is thus only on the fringe of a problem of far wider significance. As the expectation of life extends, so cases of infirmity will increase; and unless this is recognised, and the physical and mental deterioration of these infirm people prevented, hospital beds will go on being filled by patients who should never have been allowed to reach the stage of needing expert medical and nursing care.

The problem presented by the aged is primarily sociological, demanding the full coöperation of the medical and nursing staffs of hospitals, the medical officer of health and the local-authority services, and the general practitioners. All these are already playing a part, but with little attempt at coördination—because, in fact, existing legislation makes such coördination almost impossible. The appointment of geriatricians by regional hospital boards is pointless if the local authorities are unable to provide suitable accommodation for those restored to health. It may satisfy the geriatrician to fill empty wards in institutions with ambulant cases who have recovered and thus relieve his scanty nursing staff, but it can hardly excite the old person who yearns for the privacy and freedom of his own home, be it only one room. We must recognise this as a problem in social and preventive medicine.

A UNIFIED SERVICE

We know little of the process of ageing and are doing nothing to guide and advise old people so that they remain strong and healthy. Geriatricians are holding hospital outpatient sessions, but here again the emphasis is on the treatment of acquired conditions.

Cannot an analogy be drawn here with the tuberculosis service, which combines preventive and therapeutic measures in the dispensary and the hospital? Surely, besides treating and reabling the aged sick in the hospital wards, the doctor in charge ought to visit the homes and work in conjunction with the medical officer of health. In fact this doctor, instead of being employed solely by the regional hospital board, should have a combined appointment under the board and the local authority. He would then have the power to supervise the old people in the hostels and homes established by the local authority, and would be able to create a movement

Digitized by Google

between the hospital wards and the homes. The turnover of patients thus established would encourage doctors and nurses to take up this type of work. We should have, moreover, a unified instead of a divided service for old people. More beds would be freed, and old people could therefore be admitted to the wards promptly, and treated before their conditions became chronic. Clinics for the elderly might well be set up by local authorities, similar to maternity and child-welfare clinics in that their purpose would be to prevent disease. The doctor from the hospital, holding a combined appointment, would attend these local-authority clinics in company with an assistant medical officer of health. His experience would enable him to suggest ways of retarding those disabling conditions which can be prevented.

The term "geriatrician" is unfortunate, and should be discarded; it is an unattractive word, the first part of which, in spite of its Greek derivation, conjures up different images in the minds of different people, while the second part suggests that the problem of the elderly and chronic sick is solved when the medical treatment is completed, which of course is quite incorrect. The title suggests also the creation of a new specialty, which has already roused suspicion though those who are most suspicious may also be those who in the past have ignored their responsibilities. It is doubtful whether such a specialty would attract specialists of the highest academic rank; other things being equal, such doctors will prefer appointments as general physicians in which they will see cases of greater variety and interest, besides getting quicker results and more mental stimulation and satisfaction.

Are treatment and rehabilitation of the aged sick so complicated and profound as to demand the creation of another specialty? Is it desirable that membership of the Royal College of Physicians should become a condition of appointment, as might happen if the problem came to be regarded as purely clinical? Surely what is needed is the appointment of a doctor with understanding and experience, with enthusiasm and the ability to gain the coöperation of his specialist colleagues; a doctor who has had postgraduate training in the treatment of sickness in the aged from the existing specialists, and who understands the preventive and social aspects of his task. If he must have a designation there is something to be said for "gerocomist"—a word which is no more hideous than "geriatrician" and suggests a wider range of activity. But is there any need for a special title other than "physician for the elderly"?

It might be necessary for this service to be administered at regional level by a similar type of doctor, who would work under the senior administrative medical officer.

ADVANTAGES

A medical service of the kind described would have three advantages:

1. It would be welcomed by old people and general practitioners alike.
2. A combined appointment would give the doctor greater scope, and would enable him to take active steps to prevent permanent and chronic disability, and thus to save hospital beds.
3. Through the clinic and outpatient services he would bridge the gulf between the local authority and the hospital management committee. Thus the service would provide a unified medical service for old people whether they were healthy, sick, or frail and ambulant.

This increasingly serious problem can, in my opinion, only be met by a combination of preventive and therapeutic measures, with the emphasis on the former. It is a typical example of social medicine, and requires the administration of doctors who can see all its facets and who are sufficiently interested and experienced to persuade others to do their share.

CARDIAC CATHETERISATION

A HISTORICAL NOTE

A. J. BENATT
M.D. Berlin

ACCORDING to a recent estimate, cardiac catheterisation has already been performed more than 10,000 times, and it seems that this diagnostic method has come to stay.

The first to report the use of the catheter in man for obtaining mixed venous blood, and for measuring right-auricular pressure and cardiac output, were Cournand and Ranges,[1] who mention Forssman as the originator; and McMichael[2] also repeatedly quotes Forssman. The French, on the other hand, speak of "Bleichroeder's method" of cardiac catheterisation.[3]

THE PIONEERS

When Werner Forssman[4] conceived the idea of introducing a catheter into the right heart, his object was to administer emergency drugs on the operating-table in the most rapid and efficient way. He opposed intracardiac injections because of the peril of cardiac tamponade, which might arise through injuring the coronary vessels with the needle, though he does not mention whether in fact he had experienced such an accident. The first experiment was on a human cadaver, and he was amazed at the ease with which the ureteric catheter could be guided up the arm vein into the right auricle. This, he says, is explained by the favourable position of the venous tributaries, each of which forms an acute angle with the main vein, pointing always in the direction of the blood-stream. He recommended the use of the left arm for further trials, because the left innominate vein is longer than the right and approaches the superior vena cava in a smooth arc. He then carried out an experiment on himself. A wide-bore needle was inserted into an antecubital vein, through which a ureteric catheter of 4-Charriére thickness was introduced and passed with great ease to a length of 35 cm. At this point, however, his colleague who performed the operation flinched and the experiment was abandoned. A week later Forssman took matters literally into his own hands. He infiltrated his left antecubital fossa with a local anæsthetic and dissected the vein. Having passed a catheter into it, he placed himself behind an X-ray screen and watched in a mirror the passage of the catheter, which he himself manipulated into the right heart. The screening plant was obviously attached to the operating-theatre where he carried out the experiment; but to get radiographs taken he had to walk, with the catheter in position, to the radiological department, which was quite a distance away. Though the journey involved climbing stairs he had no discomfort, and he mentions only an occasional sensation of warmth similar to that felt when calcium is injected.

In his report, Forssman visualised the future applications of his method both for diagnosis and therapy. The first patient to be treated by this procedure was a woman with purulent peritonitis, who received through the catheter one litre of glucose with added adrenaline and strophanthin. After improving temporarily she relapsed and eventually died with the catheter still in the right auricle. From his observations at necropsy of this patient, Forssman indicated the possibility of the catheter entering the mouth of the inferior vena cava.

1. Cournand, A., Ranges, H. A. *Proc. Soc. exp. Biol., N.Y.* 1941, 46, 462.
2. McMichael, J. Advances in Internal Medicine. New York, 1947; *Brit. med. J.* 1948, ii, 928.
3. Mahaim, J. Rapport et mémoires sur le IIme congrès interaméricain de cardiologie à Mexico, 1947, p. 8.
4. Forssman, W. *Klin. Wschr.* 1929, 8, 2085; *Ibid*, p. 2287.

Digitized by Google

Such are the essentials of Forssman's original publication. However, in an addendum about a month later, he says:

> "Professor E. Unger informs me that Bleichroeder, Unger, and Loeb carried out the same experiment in 1912. This was published under the title: 'Intra arterielle Therapie.' He (Unger) had passed a ureteric catheter into the arm veins up to the axilla on 4 human subjects, among them Dr. Bleichroeder, and also from the thigh into the vena cava. To judge from the length of the catheter and a stabbing pain, he believes that in the case of Dr. Bleichroeder the catheter must have reached the right heart. This latter experiment was not published."

The publication referred to [5] consists of three short papers which were read separately by F. Bleichroeder, E. Unger, and W. Loeb before the Hufeland Medical Society in Berlin. Bleichroeder, who was the opener, related how, seven years before, in 1905, he had passed catheters into the arteries and veins of dogs as well as into the veins of human beings; but as he did not believe those experiments to be of any practical value he left them unpublished. Now, in 1912, however, the opening of the chemotherapeutic era seemed to suggest a use for his method; for it was held that a chemotherapeutic agent should be applied as near as possible to the diseased organ. So, in 4 patients with puerperal sepsis, Bleichroeder and Unger inserted a catheter into the femoral artery, passed it up to the bifurcation of the aorta, and injected 'Collargol' through it.

In his paper Bleichroeder did not disclose the exact nature and object of his experiments carried out in 1905, but merely remarked that he used the catheter to obtain blood from the inferior vena cava in the neighbourhood of the hepatic vein for some metabolism investigations. From publications by him in 1904 on the morbid anatomy of cirrhosis of the liver [6] it might be inferred that he employed it in connexion with this study; but so far I have been unable to trace a report of the results. In his address on intra-arterial therapy, he stated that in dogs he had passed the catheter through the femoral vein well over a hundred times, and had left it in position for several hours without clot formation or other ill effect. Bleichroeder then described how on two occasions the catheter was introduced by Unger through a vein of Bleichroeder's forearm and passed up to the axilla; no side-effects were noticed in these two or in three other experiments on different subjects. Finally he said that in 1905 a catheter was inserted into one of his thigh veins and directed into his inferior vena cava.

PRIORITIES

Forssman presented his paper well, performed his experiments in logical sequence, carried them out with zeal and great courage, and provided radiological evidence that the tip of the catheter had reached the right auricle. Moreover, he was the first to inject a radio-opaque substance directly into the right heart [7]; but, though producing exemplary skiagrams of dogs, he did not succeed in obtaining contrast pictures of his own heart when he injected 'Uroselectan' through the catheter, which this time was inserted, after Bleichroeder's example, via his thigh veins.

Bleichroeder, on the other hand, could hardly be expected to have achieved radiological control in his experiments for in 1905 the use of X rays was in its infancy. Thus his work was carried out under even greater difficulties than Forssman's, and the courage with which it was undertaken cannot be regarded as less conspicuous. In fact, by guiding a catheter through the thigh veins into the inferior vena cava, Bleichroeder went a step further than Forssman. His paper does not mention how far the catheter was inserted, and therefore the evidence that the instrument actually reached the right auricle is not strong, but he did at least prove that a ureteric catheter can be introduced into the veins and arteries of man without danger of pain, clotting, or other major complication. Though Forssman may have been unaware of it, Bleichroeder's work did not remain unknown; for Christeller and Eisner,[8] who employed the catheter in experiments on dogs, quoted Bleichroeder and Unger as the originators of the method—a claim which Bleichroeder himself never made in respect of animals.

It appears therefore that Bleichroeder deserves credit for being the first to pass a catheter into the veins and arteries of man, while Forssman must rank as a pioneer of cardiac catheterisation mainly in its application to modern angiocardiography.

THE TWO MEN

Fritz Bleichroeder was medical director of a small hospital for women in Berlin. His early interest was in the morbid anatomy of cirrhosis of the liver. In this field he made important contributions, some of which accord with present-day knowledge. He was a man of considerable wealth, but he was very modest and unassuming, and was hesitant about publishing his experimental results. This may account for the long delay in presenting his observations with the cardiac catheter and the absence of more detailed publications on these studies. He has been repeatedly described as of noble and upright character. Under the Nazi rule he had to relinquish his hospital post, and when conditions became unbearable he decided to emigrate to Australia; but he died before embarking on the journey.

Little is known about the fate of Forssman: the last information dates back to 1944, when he was assistant surgeon at one of the large hospitals in Berlin. His first experiments, reported in 1929, were carried out at a hospital in Eberswalde, a town about 50 miles north-east of Berlin. Soon after he had completed his work on cardiac catheterisation, he went as registrar to the surgical department of the Charité in Berlin under Sauerbruch, but in 1931 returned to Eberswalde, where he made his first studies on angiocardiography. There is no evidence that he pursued this problem any further; his subsequent papers deal chiefly with urosurgical subjects.

5. Bleichroeder, F. *Berl. klin. Wschr.* 1912, **49**, 1503.
6. Bleichroeder, F. *Virch. Arch. Path.* 1904, **177**, 435; *Disch. med. Wschr.* 1904, 409, 481, 521.
7. Forssman, W. *Münch. med. Wschr.* 1931, **78**, 489.
8. Christeller, E., Eisner, G. *Zieglers Beitr. Path. Anat.* 1928, **81** 524.

HEALTH PROGRAMME FOR THE U.S.A.

PRESIDENT'S MESSAGE TO CONGRESS

IN a message to Congress last week, proposing a nation-wide health programme, President Truman recalled that in a special message on Nov. 19, 1945, and in a number of messages since then he recommended the enactment of comprehensive legislation to improve the health of the nation. The issues involved in these recommendations, he said, have been debated all over the country, and a large measure of agreement has been reached. "There has been increasing recognition of the need for positive, planned action to bring adequate health services within the reach of all our people. With respect to most of my recommendations, there is no longer any substantial difference of opinion."

Legislation already enacted is helping substantially to provide better health services and medical care. "For example, federal funds are now being made available to help in building badly needed hospitals; the federal government's programmes of medical research have been expanded; and additional grants have been made available to the States to aid in establishing and maintaining public-health services.

"However, the action thus far taken falls far short of our goal of adequate medical care for all our citizens. If we are to deal with the problem realistically and in its true dimensions, action is required on a broader scale."

Digitized by Google

Technical resources have greatly increased, but "as a nation we have not yet succeeded in making the benefits of these scientific advances available to all those who need them. The best hospitals, the finest research laboratories, and the most skilful physicians are of no value to those who cannot obtain their services."

"Our objective must be twofold: to make available enough medical services to go around, and to see that everybody has a chance to obtain those services. We cannot attain one part of that objective unless we attain the other as well." The country is short of physicians, dentists, nurses, medical technicians, and public-health workers; it needs more hospitals and clinics; medical personnel and facilities are unevenly located in relation to needs and are practically deficient in rural areas. "We need broader, better-supported medical research. We need much more attention to preventive health care and more adequate public-health services. Most of all, we need more widespread use of the modern method of paying for medical care through prepaid insurance."

HEALTH INSURANCE

"My first recommendation is that the Congress enact legislation providing for a nation-wide system of health insurance. The traditional method of paying for medical care cannot meet the health needs of today. As medical education and practice have become better, they have become more specialised and at the same time more expensive. . . . It is no longer just the poor who are unable to pay for all the medical care they need—such care is now beyond the means of all but the upper-income groups. This is an anomalous situation. It can and should be met through social insurance. Under such a system, regular contributions to the insurance fund will replace irregular, often overwhelming, family outlays for medical care."

The growth in recent years of insurance against the costs of medical care is proof that the people understand the advantages of health insurance and desire its extension. Unfortunately, however, voluntary plans have proved inadequate; only $3^1/_2$ million people have insurance which provides anything approaching adequate health protection. Most serious of all, those who need protection most cannot afford to join.

"The only fair and effective means to assure adequate medical care through insurance is to build on the pattern of our existing social-insurance plans. As in the case of those plans, we should seek to include as many persons as possible within the health-insurance system, so that more may benefit and costs can be more widely shared. Health insurance . . . will not require doctors to become employees of the government. . . . Moreover, patients, doctors, and hospitals will remain free to make their own arrangements for care outside the insurance system if they so choose.

"The administration of the programme should, of course, be decentralised to the greatest possible extent. It is also of the utmost importance that the individuality of medical care be adequately safeguarded. Both these objectives can be accomplished in large measure by having the administration of the programme in each locality guided by a local group in which the skills and judgment of local medical personnel are fully represented."

MORE PERSONNEL

The President's second recommendation is that Congress enact legislation to help medical schools expand. Special financial aid should be provided for the construction of teaching hospitals and other facilities and to help the schools cover the cost of larger enrolments. At the same time scholarships should be provided for good students who might otherwise lack the means to undertake professional training.

"Today we have about 190,000 active physicians, of whom 145,000 are in private practice. This is not enough; it represents only about 80% of the physicians we require. Unless we take prompt action to expand the medical schools, we shall be no better off ten years from now. We face similar shortages with respect to dentists, nurses, and other professional medical personnel."

Comprehensive health insurance will lead to a more equitable distribution of doctors; "and we will no longer have the situation where some counties have only 1 active physician for every 3000 persons, while other counties have 5 or 6."

INCREASING THE RESOURCES

The President's third recommendation is that the federal government provide increased aid for the construction of hospitals and other medical facilities in communities where they are needed. "Under present circumstances hospitalisation is often impossible, both because of the shortage of hospitals and because of inability of the patient to pay the cost of hospital."

The federal Hospital Survey and Construction Act, passed in 1946, represents an important step in a national programme to provide more hospitals. Under this Act, expiring in 1951, some funds are provided for the government to contribute one-third of the construction cost of public and other non-profit hospitals.

"I recommend that the Congress extend the duration of this programme, increase the funds to be made available, and modify the programme so that the government's share will take account of the varying financial resources of different States. Furthermore, the programme should be broadened to include aid for the establishment of community health centres, diagnostic clinics, and group-practice clinics, all of which have proved in recent years to be very effective means of providing better medical care."

PREVENTIVE SERVICES

At present the government provides grants to assist State and local governments in preventing and controlling certain diseases and to promote maternal and child-health services for crippled children, and general public-health activities. The President's fourth recommendation is that Congress should increase the amount of the federal grants for these activities, consolidate the existing separate grants in so far as possible, and provide for matching by the States adjusted to their differing financial resources. Another essential step, the President added, is to continue to improve medical research.

RELATION TO OTHER SOCIAL LEGISLATION

"These recommendations . . . present a sensible and realistic programme of action, which complements my recommendations for extending and improving the social security system, including the provision of insurance against loss of workers' incomes during periods of sickness or disability."

"Many people are concerned about the cost of a national health programme. The truth is that it will save a great deal more than it costs. We are already paying about 4% of our national income for health care; more and better care can be obtained for this amount of money under the programme I am recommending."

Mr. Truman's message refers to a Bill introduced last Monday to the Senate and the House of Representatives. Under this measure, which is based on a report by Mr. Oscar Ewing, chief of the Federal Security Administration, 1·5% would be levied on all earnings up to $3600, with an equal contribution from the employer; the remainder of the cost would be met by the federal government out of taxes. A less radical measure, introduced by Senator Taft, would authorise federal grants to the States for the extension of medical

Digitized by Google

and hospital services, without introducing national insurance.

Of Mr. Truman's message and the Bill he advocates, the *Manchester Guardian* (April 25) observes: "The main controversy will turn on the question of compulsory insurance, . . . rather than on the method of paying the doctors." And the Washington correspondent of the *Times* (April 26) writes:

> "The American Medical Association—a body beside whom the Bourbons would have seemed dangerous innovators—said yesterday that the health of the American people 'would be seriously endangered if this Old World scourge is allowed to spread to our New World,' adding that 'it is the discredited system of decadent nations which are now living off the bounty of the American people.'"

IMPERIAL CANCER RESEARCH FUND

AT the annual general meeting held on April 20, Prof. H. R. Dean, who presided, presented the annual report of the fund. Besides describing the observations of Professor Gye, Dr. A. M. Begg, Dr. Craigie, and Miss Ida Mann which are reviewed in our leading article, the report gives an account of other investigations in progress.

From the work of Dr. L. Foulds it now appears that the virus of mouse mammary cancer is transmitted by the father's sperm as well as by the mother's milk, for the progeny of hybrids from low-breast-cancer mothers and high-breast-cancer fathers develop a high proportion of cancers. It is now accepted that mouse mammary cancer requires the combined interplay of three factors—a genetic factor, a hormonal factor, and the viral milk factor.

Dr. Foulds is also working on the "natural history of cancer" or "progression"—i.e., the changes in the characteristic growth-rate and responsiveness to hormonal stimulation of tumours. Some of the mouse breast tumours grow to a maximum at the time of parturition of the host and then regress almost completely until the next pregnancy, when they grow vigorously again at the same site. The progression is not brought about by the host but is due to fluctuations in the tumour; it is independent of the growth of other tumours in the same animal and of the previous biological history of the tumour, and the growth-rate and responsiveness alter independently. "The behaviour of tumours is the resultant of several characters which vary, within wide limits, independently of each other and undergo independent progression. The characters include growth rate, invasiveness, capacity for dissemination, and responsiveness to environmental stimuli, of which the hormones are the most easily recognised, but not necessarily the only examples."

Dr. Beatrice Pullinger is studying the Bittner milk factor and the relationship between spontaneous and chemically induced mammary cancer. Dr. E. Vazquez-Lopez, in testing the inhibitory effect of thiourea on the formation of mammary tumours in mice of R3 strain, has come to the conclusion that the effects can be better explained by a fall in cancer incidence of the progression type described by Foulds. The fall in the mammary-cancer rate of the R3 strain was more than compensated by a great rise (60% incidence) of lymphomas in the females.

Mr. H. G. Crabtree has studied the carcinogenesis of liver tumours induced by dyestuffs of the type of *p*-dimethylaminoazobenzene. With many other workers in this field, he still maintains that this carcinogenic process can be explained by reference to the metabolic products of the carcinogen. He has made the remarkable observation that some of the azo compounds, on administration to the rat, act as growth stimulants.

Dr. C. C. Spicer is investigating the incidence of human lung cancer genetically and statistically from a study of the records of the Registrar-General and of the teaching hospitals. Mr. P. C. Williams has elaborated the technique of working with ova taken directly from the rat fallopian tubes for endocrinological investigation.

Dr. James Craigie, F.R.S., is to be director of the fund after Professor Gye's retirement in August.

Public Health

FEVER WITHOUT RASH AFTER CONTACT WITH SMALLPOX

IAN R. GRAY
M.B. Lond., M.R.C.P.
LATE GRADED PHYSICIAN, R.A.M.C.

Two more or less distinct phases may be recognised in the course of smallpox—that of pre-eruptive toxæmia, and that of rash. Though it is often brief and mild, the pre-eruptive toxæmia may be very severe, and death may take place before the rash appears.

Though severe toxæmic symptoms are usually followed by a profuse eruption, this is by no means always so. A well-marked pre-eruptive fever may precede quite a mild rash. This is especially likely when immunity induced by vaccination is wearing off. It has long been recognised (Ricketts 1908) that the immunity to smallpox induced by vaccination consists of two factors—one modifying or preventing the cutaneous lesions, and the other resisting the toxæmic manifestations of the disease. As time passes, these two immune reactions become gradually less effective, but immunity to toxæmia is lost more rapidly than immunity to the skin lesions. In the gradual loss of vaccinial immunity there is probably, therefore, a phase during which there is susceptibility to the pre-eruptive fever of smallpox and yet at the same time complete or almost complete immunity to its cutaneous manifestations.

The non-eruptive form of smallpox which follows infection during this phase has been termed contact fever, variola sine exanthemate, or variola sine variolis. It has no characteristic clinical features and is usually only recognised in the course of an epidemic. Though the diagnosis has not yet been proved by virus studies, one case described showed strongly suggestive serological evidence of infection with variola (Conybeare 1946), and the clinical circumstances of the other reported cases leave small doubt about the nature of the illness.

For example, Conybeare (1939) and Mellows (1938) reported 7 cases among 16 persons who had been in contact with a single patient with smallpox: all had been successfully vaccinated in the past. Flandin's (1942) 10 cases occurred in previously vaccinated patients after contact with smallpox in the pre-eruptive stage in a hospital ward; and 6 similar cases were described by Howat and Arnott (1944).

Contact fever is commonly diagnosed initially as influenza, the symptoms being headache, backache, pains in the joints, muscular soreness, and sometimes nausea and vomiting. It is usually only when several cases are seen and the exposure to infection is obvious that the diagnosis is made. The apparent incubation period—using this term to mean the length of time between exposure to infection and clinical onset—has been variously reported as between three and eighteen days, but most observers place it between ten and fourteen days—i.e., the same as that of variola.

Eruptions similar to the non-specific prodromal rashes of smallpox may occur (Conybeare 1939, Boul and Corfield 1946), and in 6 out of 7 cases reported from the Middle East "vague rounded shadows in the lower lung fields" were seen in X-ray films taken during the fever (Howat and Arnott 1944), though no symptoms or physical signs were referable to the chest. The duration of the fever is between two and seven days, and the only recorded residual disability is lassitude lasting for several weeks (Conybeare 1939).

Digitized by Google

Precise reports of the state of vaccination in all reported cases of contact fever have not been published, but it is striking that every patient reported had been successfully vaccinated at some time in the past, and that successful vesiculation has never been obtained when the patient has been revaccinated during the incubation period of, or convalescence after, the fever. The interval between successful vaccination and susceptibility to contact fever has been several years in all cases in which it is mentioned. This supports the conception that contact fever is smallpox modified by a fading vaccinal immunity, and is at variance with the statement that the condition is apt to be encountered among recently vaccinated persons exposed to smallpox (Rolleston and Ronaldson 1940).

CLINICAL REPORT

During March and April, 1948, there was a small but severe outbreak of smallpox among Mauritian troops in North Africa. The patients were admitted to a British military hospital. The first two patients, admitted in the pre-eruptive stage, were watched for one and two days before a diagnosis was reached. They were then transferred, and all subsequent cases were admitted, to an improvised isolation hospital. Of 11 of the hospital staff who were in contact with these patients during the course of their illness 5 subsequently developed contact fever. As soon as smallpox was recognised the whole hospital staff were vaccinated. Only 3 had been in close contact with smallpox before being vaccinated; these were the medical officer in charge of the cases and two nursing orderlies. Between ten and fourteen days later all 3 developed fever. The 2 others who developed contact fever were a nursing orderly and the cook who was at the isolation hospital.

The incubation period could not be assessed accurately, because in no instance was there only a single exposure to infection. It appeared to lie between ten and eighteen days, but in 3 persons it was almost certainly between ten and fourteen days. Infection in the latter was probably from patients either in the pre-eruptive or very early eruptive stage.

The onset of symptoms was abrupt, with malaise, headache, shivering, and aching in the limbs. There were mild respiratory symptoms in 4 cases, with slight coryza in 2, and pharyngitis and bronchitis each in 1; 3 had conjunctival injection in the early stages. The temperature rose to about 100°F on the first day, reaching a maximum of 103° or 104°F usually on the third day. In 1 case fever lasted only three days, but in the other 4 it lasted five or six days. In no case was enlargement of spleen or lymph-glands observed. Only 1 patient had chest signs, and then only of bronchitis. No cutaneous lesions were seen. Blood-culture was sterile on the one occasion it was attempted; the leucocyte-count in this patient was 4000 per c.mm. (polymorphs 57%, lymphocytes 31%, mononuclears 7%, eosinophils 5%).

The absence of characteristic clinical features in a contact-fever illness makes the diagnosis uncertain. Alternative causes of pyrexia, such as sandfly fever and influenza, are rare in this part of North Africa and would be particularly uncommon in spring. No other cases of undiagnosed pyrexia were treated in the military hospital during the period in question. It therefore seems significant that, after exposure to smallpox in its early stages, 3 men should fall ill within a period of forty-eight hours some twelve days later.

STATE OF VACCINATION

The vaccination histories of the members of the staff exposed to infection were as follows.

Case no.	*Vaccinations*	*Earliest possible exposure*	*Onset of fever*
1 ..	Ch +, 1945 +, 1946 −, 1947 −, April 2, 1948, −	March 30 ..	April 12
2 ..	Ch +, 1947 −, April 2, 1948, −	March 30 ..	April 10
3 ..	Ch +, 1947 −, April 2, 1948, −	April 1 ..	April 10
4 ..	1929 +, 1947 −, April 3, 1948, −, April 10, 1948, −	April 3 ..	April 25
5 ..	1946 +, April 3, 1948, −, April 10, 1948, −	April 3 ..	April 18
6 ..	Ch +, April 2, 1948, + ..	April 10 ..	—
7 ..	Ch +, April 2, 1948, + ..	April 11 ..	—
8 ..	Ch +, April 4, 1948, + ..	April 11 ..	—
9 ..	1946 +, April 2, 1948, (M), April 10, 1948, −	April 3 ..	—
10 ..	1947 +, April 2, 1948, − ..	April 3 ..	—
11 ..	1947 +, April 2, 1948, (M) ..	April 3 ..	—

Ch, childhood. +, vesicular response. (M), accelerated response. −, no response.

All those who developed contact fever had had a successful vaccination two, three, or more years previously but had not "taken" on revaccination both in the intervening period and at the time exposure started. None of those who had had a successful vaccination immediately before exposure to infection developed fever. Of the 6 who were exposed to infection and did not develop fever 3 had had successful vaccination a few days before being exposed and the other 3 had been vaccinated one or two years previously. No cases of contact fever or any other pyrexial illness were diagnosed in the unit from which the smallpox came. This unit was isolated and under close medical supervision during the two weeks following the outbreak It consisted of coloured troops and had been formed a year before from newly enlisted men, who were said to have been vaccinated successfully at that time. Nevertheless a high percentage of successful revaccinations was obtained at the time of the smallpox outbreak. Why none of the close contacts in the unit developed fever cannot be explained. Possibly the immunity to smallpox induced by vaccination in coloured races may be different in some respects from that in Europeans.

SUMMARY

Of 11 doctors and nurses in contact with smallpox at a hospital, 5 developed contact fever. They had fever accompanied by headache, shivering, aching of the limbs, and in some cases mild respiratory symptoms.

The incubation period was between ten and fourteen days in 3 cases and was uncertain in the other 2. The pyrexia lasted from three to six days.

All those who developed contact fever had given a vesicular response when vaccinated two or more years previously but had not responded to revaccination at the time of exposure. None of those who gave a vesicular response when vaccinated shortly before exposure developed fever.

These observations suggest that those who developed fever had immunity to the cutaneous lesions of smallpox and possibly therefore could not give a vesicular response on revaccination, but had lost their immunity to the toxæmia of smallpox, thus sustaining smallpox without rash when infected with the virus.

I wish to thank Dr. C. G. Parsons, lately consulting physician to the M.E.L.F., and Dr. E. T. Conybeare, of the Ministry of Health, for their valuable assistance with this paper, and the Officer Commanding B. M. H. Benghazi and the Director-General, Army Medical Services, for permission to publish it.

REFERENCES

Boul, W. T. G., Corfield, W. F. (1946) *Lancet*, ii, 284.
Conybeare, E. T. (1939) *Ibid.*, i, 813.
— (1946) *Practitioner*, 157, 191.
Flandin, C. (1942) *Bull. Soc. méd. Hôp. Paris*, 58, 99.
Howat, H. T., Arnott, W. M. (1944) *Lancet*, ii, 312.
Mellows, P. B. P. (1938) *St Bart's Hosp. J.* 45, 155.
Ricketts, T. F. (1908) The Diagnosis of Smallpox. London.
Rolleston, J. D., Ronaldson, G. W. (1940) Acute Infectious Diseases. London.

Digitized by Google

Smallpox

The period of surveillance of passengers and crew of S.S. *Mooltan* expired on April 19. In England and Wales the total number of confirmed cases of smallpox arising from the fatal case on board is 11. The date of onset and of removal to hospital of these cases are as follows:

Place	Onset April	Removal April	
Port of London	3	3	Died
Paddington	5	7	
St. Pancras	5	8	
Isle of Axholme	5	7	Died
Paddington	6	10	Died
Liverpool	6	16	
Wembley	7	9	Died
Sutton and Cheam	7	11	
Torquay	8	10	Died
Aylesbury	11	13	
Richmond	12	14	

Of the 5 fatal cases 4 were in people who were unvaccinated at the time of infection, the 5th being a man of 61 who was vaccinated in infancy. In other cases there is evidence that vaccination has produced considerable modification of the disease, and this has sometimes given rise to difficulty in diagnosis. It is advisable that all contacts developing suspicious spots should be isolated for observation and bacteriological examination.

Contacts with suspicious lesions have been admitted to hospital as follows:

Place	Onset April	Removal April
Southwark	9	11
Sutton and Cheam	19	20
Romford	17	21
St. Pancras	20	23
West Ham	20	22

Up to April 25 there has been no confirmation of the diagnosis of smallpox in any person who was not on board S.S. *Mooltan*. Further investigation has removed any suspicion that the 2 patients in Laceby Smallpox Hospital mentioned last week are suffering from smallpox.

Influenza

The number of deaths (provisional) ascribed to influenza in the 126 great towns of England and Wales in the week ended April 16 was 95, compared with 192 in the preceding week. The peak figure of 360 deaths was reached in the week ended March 19, and since then there has been a fairly rapid decline. Notifications of acute primary and influenzal pneumonia reached a peak of 918 cases in the week ended March 12 and have since declined to 522 in the week ended April 9. No reports of outbreaks have been received recently, and it would appear that the outbreak of virus influenza is now over. It was characterised by high incidence in the Midlands and North but low fatality.

There were a number of isolations of a strain of virus A nearly related to the strain isolated in this country in 1947. There were a few isolations of virus B from outbreaks in semi-closed communities.

Births and Deaths

Figures for England and Wales in the first quarter of this year [1] include two health records. These were:

1. The number of stillbirths registered during the three months was 4418, giving a rate of 23·1 per 1000 total live and still births, the lowest rate ever recorded for a March quarter in this country. For the same period a year ago the rate was 24·3, and there has now been a progressive fall in the rate for the first quarter for the past nine years.

2. The number of deaths of children under 1 year of age was 7462, representing a record low rate for the first quarter of 40 per 1000 related live births. This compares with the previous record of 41 in the corresponding quarter a year ago and 55 in the March quarter of 1947.

There was again a drop in the number of live births. For the quarter ended March 31 this year the figure was 186,561, compared with 202,184 in the first quarter last year and 241,530 in the first quarter of 1947. The corresponding rates per 1000 total population were 17·4, 18·7, and 22·8 respectively.

1. The Registrar-General's Weekly Return of Births, Deaths, and Infectious Diseases for the week ended April 16, 1949. H.M. Stationery Office. Pp. 20. 6*d*.

There were 161,279 deaths, representing a death-rate of 15·0 per 1000 total population, compared with 132,705 deaths and the record low rate of 12·3 in the March quarter, 1948, and 181,736 deaths and a rate of 17·1 in the corresponding quarter of 1947.

Parliament

QUESTION TIME

Access to Hospital Records

Mr. JOHN LEWIS asked the Minister of Health if he was aware that the senior administrative medical officer of the Manchester regional hospital board had instructed medical officers at venereal-disease clinics in the area that information about patients attending the clinics should not be disclosed to medical officers of health, even if requested for purposes of contact tracing; and, in view of the fact that medical officers of health in all parts of the country had always had free access to information about patients, which they had treated with confidence, if he would take steps to have this instruction withdrawn forthwith.—Mr. ANEURIN BEVAN replied: The regional hospital board has rightly taken this step to ensure that the statutory regulation about secrecy of V.D. treatment is scrupulously observed. Mr. LEWIS: Is the Minister aware that in the interests of an efficient health service it is vital that there should be the same free access to information by medical officers of health which they have had in the past not only for the essential purpose of contact tracing, but in order to ensure that proper aftercare attention can be given to children whose mothers are known to have suffered from this disease?—Mr. BEVAN: It is not necessary for this purpose that there should be a disclosure of clinical details to medical officers of health. The patient's own doctor is, of course, made aware of all the circumstances. Mr. LEWIS: How can health visitors deal with these matters unless they know the facts of the case?—Mr. BEVAN: The man's own doctor will be aware of all the facts of the case, and as the man's own doctor is a family physician, he will be concerned about the welfare of the children. Mr. LEWIS: This is very unsatisfactory.

Mr. LEWIS asked the Minister if he was aware that the senior administrative medical officer of the Manchester regional hospital board had advised the secretary of the Bolton hospital management committee that if medical officers of health asked for information about patients who were discharged from hospital and were in need of aftercare, only the address need be given; and, in view of the fact that aftercare attention was often necessary and that children classed as handicapped were entirely the responsibility of the local authority, if he would take steps to cancel this instruction.—Mr. BEVAN replied: I understand that the board has encouraged management committees to coöperate fully with local authorities but has rightly advised them not to disclose to them clinical details of patients which should generally be treated as confidential. Mr. LEWIS: Will the Minister bear in mind that under the National Health Act there is a responsibility on local authorities in respect of aftercare work, and to refuse medical officers of health any information other than the address is to reduce them to the level of laboratory assistants which will have a deleterious effect on the whole health service?—Mr. BEVAN: My hon. friend is attributing a status to the medical officers of health which they themselves do not claim. He ought not to refer to them in such terms. It is undesirable that there should be a general access to clinical details of patients' conditions. It is only necessary for that to be done where tracing is absolutely essential.

Sale of Medical Practices

Dr. S. SEGAL asked the Minister whether he was aware that medical practices were still being advertised by private agencies for sale and purchase, and what steps he proposed to take to put an end to this practice; and whether he could now make arrangements to establish official agencies for the transfer of medical practices, partnerships, and assistantships.—Mr. BEVAN replied: There is no prohibition on the sale and purchase of purely private practices and I see no objection to such transactions being handled by private agencies. The transfer of practices, and the introduction of new partners and assistants, in the National Health Service, are already controlled by the appropriate official bodies.

Digitized by Google

Emergency Patients

Mr. EDGAR GRANVILLE asked the Minister under what authority a doctor refused to attend a person who was not his patient in a case of extreme emergency; and if, under his present rules, doctors might refuse to attend patients for personal reasons, such as the lateness of the hour.—Mr. BEVAN replied: A practitioner in the National Health Service is required to comply with the terms of the local arrangements regarding treatment in emergency. The executive council have power to exempt particular practitioners on grounds of age or infirmity, or where they have limited lists from liability for emergency night calls to persons not on their lists.

State Payments to Hospitals

Mr. BARNETT JANNER asked the Minister how much money had been received by hospitals since their nationalisation.—Mr. BEVAN replied: The total amount advanced by my department to regional hospital boards and boards of governors in England and Wales for the period July 5, 1948, to March 31, 1949, was £114,469,380. Information is not at present available as to the amount of local receipts on Exchequer account or by way of voluntary gifts for the provision of amenities.

Distribution of Estates

Mr. RALPH ASSHETON asked the Minister whether he was aware that hardship was being caused to individuals by delays in the distribution of estates due to the obscurity of the legal provisions of the National Health Service Act, 1946; what action he proposed to take to expedite the settlement of these cases; and whether he proposed to indemnify individuals against costs incurred in this connexion.—Mr. BEVAN replied: I am aware of these cases and am taking such action as is open to me, in coöperation with the solicitors for the other parties concerned, to secure early hearings. I anticipate that a decision by the courts in the first of the two cases about which the hon. Member has written to me will greatly assist the determination of others outstanding. The question of costs is a matter for the courts.

Propyl-thiouracil Supplies

Sir IAN FRASER asked the Minister if he would make supplies of propyl thiouracil available in this country.—Mr. BEVAN replied: Propyl thiouracil is being manufactured in this country in small quantities but it is not yet established here that the drug has advantages over thiouracil and methyl thiouracil which are used for similar purposes.

Analgesia Research

Mr. PETER THORNEYCROFT asked the Lord President of the Council what research was at present being carried on by the Medical Research Council on the subject of the administration of analgesia in childbirth; whether research was going on upon the use of 'Trilene' for this object; how many types of trilene apparatus were at present being investigated; in which hospitals tests were being carried out; and what were the approximate numbers of research-workers and amounts of money involved.—Mr. HERBERT MORRISON replied: The special committee on the subject has only just been set up, and its first task will be to survey the problem before deciding what new investigations are required. The question remitted to the committee is on the possibility of devising improved or new methods of analgesia, whether with trilene or some other substance, and any examination of types of apparatus already available will be incidental.

Shortages, high prices, and too tempting displays in the shops are short-term causes to which the increase in juvenile delinquency is attributed in the joint circular sent by the Home Office and the Ministry of Education to local authorities. More deeply rooted causes, they suggest, are unsatisfactory home conditions, changing moral standards, and failure to recognise and to give early treatment to subnormal children. Whatever the reasons, the provisional figures for 1948 show that 26,715 children under fourteen were found guilty of indictable offences, an increase of 26% on 1947, and 11,118 of non-indictable offences (an increase of 36%). For young people between the ages of fourteen and seventeen the increases were 23% and 15%. The circular urges local youth organisations, welfare committees, and teachers to form representative bodies to study delinquency and to encourage remedial and preventive methods.

In England Now

A Running Commentary by Peripatetic Correspondents

MY pre-Bevan spectacles suffered a minor casualty the other day, and just as I was putting on my standby pair one of the legs snapped. The optical wallah whom I consulted assured me of his personal sorrow and added that it would take at least a month to have the repairs done. When I pointed out that, while I could see to walk and could probably differentiate between a bus and a pedestrian, I would find it impossible to read anything less than a poster saying Come to Blackpool, he was not very helpful. "It will take about three months to get another pair under the scheme," he was explaining, when I suddenly said, "I'll manage after all. I've just remembered I have another pair." Perhaps the tense was wrong, but my intention was right. Along the street stood one of our large chain stores, one of the awful culprits of the prescientific era, where one could select a pair of glasses from a tray, try them on, and go on trying on, pair after pair, till one's eyes were well and truly satisfied. Within a quarter of an hour I emerged from its swing doors with two pairs of glasses—one for ordinary use and one for reading. It is all very unprofessional of course; but, apart from the handiness of my bifocals, I am very well pleased, and just a bit sceptical about the danger of handpicked specs, particularly for older folk like myself.

* * *

Readers of your timely but alarming leading article of April 16, on the toxicity of the new insecticides, may like to be reminded of the original insecticide—unique, safe, speedy, and effective—namely, *Volucres insectivores*. These, to function effectively, merely require house-room, in hedges and copses; the house-building they manage for themselves. The further destruction of hedges and copses should therefore be steadily resisted.

* * *

To return for a moment to the quintessence of the ideal general practitioner. It is entirely elusive, indefinable, and unteachable, but I would put it to the young doctor like this: if you can tell your patient the most brutal truths about himself in such a way as to make a lifelong friend of him, and let him feel that you have conferred a privilege in giving him this confidence, you have reached the summit of usefulness in general practice.

In hospital, a tricky differential diagnosis may be the principal headache; in general practice, it is seldom more than a useful academic exercise, for ultimate diagnostic responsibility rightly belongs to the specialist. The general practitioner is not usually tested by what he knows, but by what he is. He may be told what to do, but no-one will attempt to teach him how to do it—how, for instance, to mitigate a distressing verdict.

The less there is for him to do as a doctor, the more the patient will depend on how he does as a man. With a verdict of cancer, or progressive deafness, or mongolism in an only child, medicine shuts her doors and bids the doctor turn to some quality within himself, if he would help his patient through the crisis.

Again, I would say to the young doctor—if you have nothing else to give, give friendship. The disinterested friendship of a person one respects is an anodyne that can reach every affliction, and no-one need doubt your disinterestedness today. You can enrich your friendship enormously by basing it on some quality in your patient which he barely suspects, but which is revealed to you in the intimacy of a privileged relationship. If you make a direct appeal to a person's courage, in friendship, he will not let you down. Tactful hints, on the other hand, will get a poor response; for they are not the usual currency of friendship, and they testify to your fear of cowardice, rather than to your trust in courage. All too often, the patient secretly shares your fears, and he will add to his troubles by trying to smother them. You cannot make a hero out of a coward merely by treating him as a brave man; but you can transform the coward into a man who accepts his weakness and deals with it bravely.

Most of us are guarding some skeleton in the cupboard, and fear of one sort or another is a fairly regular incubus. Most of us would be only too glad to have the skeleton shown off as a harmless bag of bones, barely worth the

Digitized by Google

anxiety and vigilance with which we are barricading it from the public gaze. All of us, I think, are prepared to relax vigilance in a crisis, if only some-one were at hand to show us how to break through the barrier, and to help us come to terms with what lurks behind.

The crisis is the family doctor's unique opportunity, and it need not be as serious as cancer, or as spectacular as a major operation. It arises whenever an individual's powers are overtaxed, when he needs to be made receptive to outside help. The family doctor is both privileged to look behind the barrier and authorised to pronounce on what lies behind (if he is on the spot and can pronounce reassuringly, the crisis is over). What usually lies behind is the real person, stripped of his defences, and far more lovable in his acknowledged weakness than ever he was in his assumed strength. Such weakness need not shun support, and therefore does not shun blows. The patient himself feels as if he had been given new strength, and so in a sense he has; resignation is more restful than anxiety, and surrender preferable to a losing battle. But there is something more; in saying, "I shall be ready to go, doctor, when you tell me" he has achieved dignified surrender which has more in it of victory than of defeat. Who shall say that medicine, in shutting her last door, has failed?

* * *

A year ago we started our chicken-keeping by converting a large wooden corn-bin into a henhouse and sending off an order for some March-hatched birds. Late one evening the railwayman delivered a cardboard box which gave out a delicate whistling noise. To please our children we named the four chicks inside the box after the Brontë family: Charlotte, Emily, Anne, and (as we were lucky and they all turned out to be hens) Bramwellina! All went well. The Brontës liked their house, and in due course started egg-laying. Then, one morning, the blow fell. Emily jumped down from the perch, rushed outside into the pen, laid an egg, and died. So we put the egg in the larder, and Emily in the toolshed. Such sudden death demanded investigation, and at necropsy we found marked venous congestion; the heart was normal, and the liver grossly enlarged, but we couldn't find any kidneys.

Next day I met the hospital pathologist in the corridor. He is a nice, friendly sort of chap, and when I said I had brought along a liver, he just said "do you want it sectioned?" without a murmur. We think it was leukæmia, but the sections are rather puzzling. I doubt whether Mr. Bevan realises what a range of pathological services he is providing.

* * *

It was a bit of a shock when it was brought home to me this week that if I were the mother of an ailing child I would certainly not be my G.P.'s model patient. The other day my car, less than a year old and already far more advanced than other cars six months older, suddenly produced a high temperature together with massive oil spots spreading over the engine. Immediately I rushed to the garage. Was it serious? Would it spread? How long would it take to find out the trouble? Was it due to anything I had done? But motor mechanics are more insensitive to the appeals of a distracted mother than I am. For instance, I never tell her that her darling's oil, I mean red spots, and high temperature are due to overworking, though I may suggest they are due to overeating. Why doesn't my garage man spirit away the symptoms with the mechanical equivalent of calamine lotion and cooling mixture! Instead I'm told it's the Easter holiday, the car is in a pretty bad state, it will take several days to get the required parts, and I'll have to wait. Sadly I return home, my legs aching with the thought of unaccustomed exercise. The day drags on, evening comes. There's one thing I can do. I can phone up the garage again or perhaps pop round myself to inquire how things are going. I know it is long past surgery, I mean closing-time, and I have already phoned three times, but my car isn't like other cars and there are two new symptoms I'd forgotten to mention and they had better be treated at the same time. Anyhow I'm sure the man ought to be told of them at once. He can't mind me asking and if he has chosen tonight of all nights to go to bed early it's just too bad.

Letters to the Editor

SPECIALIST APPOINTMENTS

SIR,—With reference to "Registrar's" letter of April 2 and your reply, we should like to point out that, though everyone is agreed that more specialists are needed for the desired expansion of the hospital specialist services, the recent economy cuts in the National Health Service estimates will completely prevent such expansion. This will be so for the following reasons, some of which are already operative:

1. Postgraduate supernumerary registrars are now paid by hospital management committees, and, because their payment was not budgeted for, no new ones are being taken on, while existing ones are not having their six-month periods renewed. This last is, in some hospital groups, already causing acute anxiety among registrars. Previously, if for any reason other than unsuitability postgraduate training was to come to an end, six months' warning has been given. Now this period of grace, which affords an opportunity to look for an established post—no easy matter at present—is no longer being given, and recently three registrars in a particular hospital have had their appointments terminated with only two weeks' warning.

2. Many of the supernumerary registrars, whose services are now being dispensed with, have been doing work essential to the proper running of the hospitals—work which otherwise would have had to be done by established members of the staff if it were to be done at all.

3. When the regional hospital boards make their recommendations for the staffing of hospitals to the management committees, these will be unable to implement them.

Reasons (2) and (3) naturally follow the economies in the National Health Service estimates because management committees did not budget for the necessary money and supplementary estimates have been forbidden.

Thus not only is any extension of the hospital specialist services effectively ruled out for some time to come but probably the hospital services cannot be run as efficiently as hitherto. Apart from any consideration of hardship to the individuals affected, the present policy must jeopardise the National Health Service at its very inception. Once registrars leave the hospitals and are swallowed up in other branches of medical practice, such as general practice, they will be lost to the hospital service for good. Surely it is fantastic that the Treasury, which has spent hundreds of thousands of pounds on the postgraduate training scheme in the last three or more years, should be prepared now to throw it all overboard.

As practical measures in the present critical situation we would urge that:

1. All postgraduates should be allowed to continue in their present appointments until the recommendations of the reviewing committees have been implemented.

2. If, for economy reasons, there is no intention to implement these recommendations, this should be stated at once so as not to perpetuate the false hopes raised by previous statements.

3. Finally, if for economy reasons postgraduates must have their appointments terminated, then a minimum period of warning of six months should be given. In view of the present difficulty of obtaining medical posts, this is only just.

TWO MORE REGISTRARS.

OPERATION FOR VARICOSE VEINS

SIR,—In his article on the treatment of varicose veins during pregnancy, published in your issue of April 9, Mr. Dodd describes the use of a long needle with an abrasive head for performing retrograde injection. This is presumably the instrument originally described by Rowden Foote and prepared by Messrs. John Bell & Croyden.

It has been used in 30 consecutive cases of juxtafemoral ligation and resection of the internal saphenous vein performed in the varicose vein clinic of this hospital in the past three months; since these differ from Mr. Dodd's cases in that all were performed under local anæsthesia, the subjective symptoms are worth noting.

Digitized by Google

The method of holding the needle so as to produce scarification of the intima was demonstrated to me by Mr. Foote. It consists in bowing the whippy shaft by compressing it between the fingers and thumb of the right hand so as to force the head against the vein wall, whilst briskly moving the needle up and down inside the lumen of the vein. In 3 cases only have I been conscious of the "grating" feeling described by Mr. Dodd, but this I now consider to be most fortunate because on those same three occasions the patients have been immediately aware of a severe burning pain along the length of the scarified vein, and have begged me to cease.

I still use the needle for retrograde injection but not as a scarifier. It has a great advantage over the ureteric catheter, in that one can be certain where it is going. So often, with the catheter, one has the feeling that the tip may have passed along one of the perforating veins into the deep veins, with the increased possibility of a deep vein thrombosis.

Varicose Vein Clinic,
Metropolitan Hospital, London. E.8. S. M. RIVLIN.

TUBERCULOUS ABSCESS AT THE SITE OF INJECTIONS

SIR,—Your correspondent, Dr. Elek (April 9), commenting on the occurrence of tuberculous abscess at the site of injection of penicillin,[1] advances the theory that infection may have been due to the inoculation of viable tubercle bacilli in the penicillin solution. He suggests that the bacilli may have gained access to the penicillin powder during its manufacture, and remained dormant during storage.

We feel that this theory is untenable on two counts: (1) it is well known that the survival-time of tubercle bacilli in a moisture-free substrate is comparatively short; and (2) Solotorovsky et al.[2] and Iland[3] have studied the effect of penicillin on the growth of recently isolated strains of mycobacteria in vitro, and have shown that growth in fluid media is inhibited by concentrations of penicillin of the order of 50–200 units per ml., when a moderate inoculum of the test organism is used. With small inocula, the minimal inhibitory concentration is much less—even as low as 1 unit per ml. It is unlikely, then, that a small number of contaminating tubercle bacilli will survive the high concentrations of penicillin commonly used in solutions prepared for injection, although in this connexion it must be admitted that the action of penicillin on tubercle bacilli appears to be bacteriostatic rather than bactericidal.

As Dr. Elek points out, it is indeed curious that none of the nine known cases of tuberculous abscess complicating penicillin injection have shown evidence of tuberculosis elsewhere in the body—a feature which rather detracts from the hæmatogenous theory of infection. We can but offer as a counter to this the fact that tuberculosis of bones and joints, of accepted hæmatogenous origin, frequently occurs in the absence of an obvious primary focus.

Kent and Canterbury Hospital, Canterbury. G. B. FORBES
F. G. ST. CLAIR STRANGE.

GERMAN DOCTORS

SIR,—Letters from a friend to whom, as to his medical colleagues of the University of Marburg, I have lately been under heavy debt for help in the displaced-persons problem, could leave no-one in any doubt that the most grievous affliction of the German doctor today is his sense of isolation, of being cut off from the heart and thought of his professional brethren throughout the world.

Any having old medical journals to spare, if they would address these to any of the medical schools of the German universities, would be astonished at the response. Any who, not having contacts in Germany, might seek a more individual response, would have journals forwarded in their names if directed to this address.

50, Ebury Street, London, S.W.1. J. P. S. DUNN.

1. Ebrill, D., Elek, S. D. *Lancet*. 1946, ii, 379. Forbes, G. B., Strange, F. G. S. *Ibid*, March 19, p. 478
2. Solotorovsky, M., Bugie, E. J., Frost, B. M. *J. Bact*. 1948, 55, 555.
3. Iland, C. M. *J. Path. Bact*. 1946, 58, 495.

VITAMIN B_{12}

SIR,—One of the more interesting developments in recent work on the anti-anæmic factor is the discovery that vitamin B_{12} is produced by certain micro-organisms. Stokstad and his colleagues [1] obtained from a rod-shaped, non-motile organism material having hæmopoietic activity in pernicious anæmia, and similar activity was shown by crystalline vitamin B_{12} isolated by Rickes et al.[2] from the metabolism fluid of a strain of *Streptomyces griseus*.

In March of this year, from Dr. H. M. Walker, of Glaxo Laboratories, we received an extract derived from the metabolism fluid of a strain of streptomyces, the vitamin-B_{12} activity of which had been assayed microbiologically. With this material we have treated two previously untreated cases of classical addisonian pernicious anæmia, neither of which showed evidence of neurological involvement. In each case there was obtained a hæmopoietic response, with a typical reticulocyte crisis, equivalent to that which might be expected from an injection of a potent liver extract.

In the first case, after two doses, each containing the equivalent of 20 μg. of vitamin B_{12}, administered at an interval of fourteen days, the hæmoglobin rose from 44 to 78% in four weeks, and the red-cell count from 1,580,000 to 3,600,000 per c.mm. In the second case, after two doses of 21 μg. at an interval of ten days, the hæmoglobin has risen in the course of seventeen days from 46 to 68% and the red-cell count from 1,670,000 to 3,070,000 per c.mm. In both patients a typically megaloblastic sternal marrow reverted during treatment to being normoblastic in type.

Further experience of this anti-anæmic factor will be necessary to show whether it will provide adequate maintenance treatment for patients suffering from pernicious anæmia and whether it will prevent the development of subacute combined degeneration of the cord.

Clinical Laboratory,
Royal Infirmary, Edinburgh. D. M. DUNLOP
W. M. WILSON.

EXCRETION OF CHLORIDE AND SODIUM AFTER SURGICAL OPERATIONS

SIR,—In their interesting article of April 16, Mr. Wilkinson and his colleagues do not mention the salt loss due to sweating; commonly the patient sweats profusely during operation. It would be interesting to know the effect of variation in the environmental temperature on the apparent retention of chloride and sodium after operation. Is it not possible that a febrile patient in a hot operating-theatre may suffer from heat exhaustion?

Epping. J. L. PATTON.

"THE SNAKE PIT"

SIR,—The film of *The Snake Pit* is to be released for adult audiences. Certain parts to which objection has been taken are to be cut, but nevertheless for it to be shown at all is deplorable.

I believe few psychiatrists from the mental hospitals in this country have had an opportunity to express an opinion on the film. It is difficult to suppose that anyone with a knowledge of modern psychiatric hospitals who has worked with outpatients could have thought its release would be beneficial to the mental health services. The primary object of those engaged in psychological medicine is to persuade the patients to seek treatment in the earliest stages of their illness. Unfortunately many members of the public are still sufficiently ill-informed to suppose they will be locked up, mixed with irrecoverable patients, and put under prison discipline, and will find it difficult to leave once they have sought treatment in a psychiatric hospital. *The Snake Pit* cannot but reinforce their fears.

There can be little doubt that the magnificent production, the acting, the photography, and the keen emotional

1. Stokstad, E. L. R., Page, A. jun., Pierce, J., Franklin, A. L., Jukes, T. H., Heinle, R. W., Epstein, M., Welch, A. D. *J. Lab. clin. Med*. 1948, 33, 860.
2. Rickes, E. L., Brink, N. G., Koniusky, F. R., Wood, T. R., Folkers, K. *Science*, 1948, 108, 634.

Digitized by Google

appeal of the film will make it a financial success. This is all the more unfortunate since it will be viewed by so many, and it is so very convincing that when it is seen it will be taken to represent a true picture of mental hospitals in general, whereas it is inapplicable to the present-day English psychiatric hospitals. As a reinforcement of the press campaigns for the improvement of certain groups of mental hospitals in the U.S.A., the film may have had its genuine uses, but it can do little but harm to the mental-health policy in this country. If, as is apparently the case, the release of *The Snake Pit* is inevitable, there is yet time to insist upon a suitable preface explaining some of these points and to enlist the assistance of the press in giving the true facts about the hospitals in this country before the progress made towards the early treatment of psychiatric illness is put back by many years.

Netherne Hospital, Coulsdon, Surrey. E. CUNNINGHAM DAX.

THE GENERAL PRACTITIONER'S REMUNERATION

SIR,—The present agitation for increase in the G.P.'s remuneration seems to have a fair amount of justification, the main arguments being: (1) the alleged non-implementation of the Spens report; (2) the low rate of pay of G.P.s in relation to dentists, opticians, and pharmacists; and (3) the low rates of pay of G.P.s in relation to specialists. (As the *Times* has pointed out, if this is uncorrected it will lead to all the abler men choosing specialisation, and thus to a deterioration in the standard of general practice.)

The two methods of increasing the rate of remuneration which are most advocated are: (*a*) a graduated capitation-rate, with higher rates for the first 1000 or 2000 patients; and (*b*) a general increase in the capitation-rate. The objections to the latter are obvious and have been frequently stated. The chief objection to the former, I have not yet seen stated. It is that if by increasing the capitation-rate for the first 1000 or 2000 you provide an adequate income for G.P.s with no private practice, you will be giving at the same time this high rate of remuneration to those who also have private practice. It is obviously inequitable to pay the same rate to practitioners who devote their whole time to their N.H.S. patients as to those with whom N.H.S. patients may be a side-line.

I suggest that the graduated increase in the capitation fee be offered only to those who are engaged exclusively in N.H.S. practice. The Minister can thereby placate the demand for an increase in remuneration, and at the same time strike another and legitimate blow at private practice—as he presumably wishes to do.

London, S.W.14. J. H. S. HOPKINS.

THE GENERAL PRACTITIONER

SIR,—In the rush of the surgeries of today how many cases of serious illness can be detected in the early stages, and how many pass through unnoticed? Clinical sense and acumen can easily be dulled by a mass of insignificant work, and knowledge of the progress of modern treatment—new drugs, new methods of surgical treatment, frequently of conditions not formerly regarded as amenable to surgery—can only be acquired by brief intervals of study, either in a library, at clinical meetings or postgraduate courses, or by personal discussion of cases in consultation with specialists.

How many general practitioners today have time or energy for any single one of these activities? And what is the worth of all the brilliant skill of our specialists, and of all the wonders of modern hospital technique, if the G.P. is so rushed in his work of form-filling that he does not have time, nor the "mental climate," in which to make his early diagnosis, and so put his patient into touch with this service at a time when treatment can be really effective?

If to this unhappy state of affairs we add a training for the G.P. of "a lower academic grade" as proposed by Dr. Plesch, how will the patients ever reap the benefits of modern advances of medicine? If "practitioners should learn only what is of practical use to them"—if "teaching should be factual and should not concern itself with current problems"—it is hard to imagine general practice retaining its appeal to those men and women who, up to the present, have provided its recruits.

Assuredly the patient will be the first to suffer if his first line of defence is manned by "doctors" whose training has been of such a utility type. Lucky will be the case who is "spotted" early and referred to the appropriate consultant at a moment when his condition may be treated with the fullest hopes of success.

London, S.W.10. A. E. BERYL HARDING.

SIR,—From the letter of Dr. John Plesch and your leading article of April 2, one conclusion is painfully obvious: it is high time we had compulsory post-graduate courses for specialists and editors—conducted by experienced general practitioners. Dr. Plesch writes from the remoteness of Harley Street, and therefore perhaps may be excused; but even you, Sir, seem unable to think of general practice except in terms of serious disease. Really, Sir, you both ought to know better. The vast majority of patients who go to their doctor have a slight complaint and not a serious one (I remember the surprise of one well-known consultant when this was demonstrated to him recently), but it is not only a matter of numbers; the trivial complaints are just as important, for they provide the occasion when preventive medicine can be of most use. Not only is the patient at the curable stage but also, just because he is ill, he is interested in what to do to avoid being ill again. Nor is this all; the patient is not "the uninteresting vehicle of a fascinating disease-process" but a human being with cares and anxieties which not only contribute to his illness but also are affected by the way we treat it. In fact the doctor who understands diseases and not human beings is no use as a general practitioner.

How ridiculous, then, is Dr. Plesch's suggestion that there should be a short course for those who are going into general practice. A better course, yes; but the general practitioner needs the widest education. Let the short course be reserved for those who are intending a narrow specialty, and going to forget all knowledge outside that field in any case.

In short, Sir, I am pleading once again that we need the best men in general practice: I had hoped that this was being realised both by you and by other authorities; but the saddest fact of modern times is the amnesia of yourself and Sir Will Spens.

East Hoathly, Sussex. F. GRAY.

*** Dr. Gray misinterprets our opinions. On April 2 we were deploring the tendency to suppose that a lower grade of doctor is adequate for general practice—a tendency illustrated by Dr. Plesch's proposals for a four-year vocational course. Insisting that the practitioner must be qualified to take responsibility in cases of serious illness, and must have a continuing interest in clinical medicine, we said:

> "He must receive a broad basic training; he must have ready access to the means of diagnosis, as well as contact with the hospital consultant and specialist; he must have opportunity and time, through the provision of health centres and through increased recruitment, to apply his mind to clinical problems; and he must have suitable pay and prestige, if only to ensure that he is joined by able colleagues. Today not one of these conditions is satisfied."

It is too often perhaps forgotten that, for a long time to come, the general practitioner will have to practise curative as well as preventive medicine; but we entirely agree with Dr. Gray that he should be concerned more with people than with diseases. On Jan. 1 we wrote of two schools of thought:

> "The first holds that under modern conditions medicine dwells in the hospitals, where alone accurate diagnosis and scientific treatment of major illness is possible. According to this school the emphasis of the new service should be on hospital and specialist services, which will deal with all the illness that matters, and the rôle of the general practitioner is chiefly to feed the hospitals. The second school, on the other hand, regard the investigation and treatment of major illness as secondary to the enormous task of relieving the troubles of everyday life, and of helping people to pursue health: the heart of medicine, they feel, is in general practice, and it is at least as important to have really

Digitized by Google

good general practitioners, bringing medicine to the home, as it is to provide pleasures and palaces for patients who qualify for institutional care."

Regretting the present ascendancy of the first school we have repeatedly expressed anxiety lest conditions should be perpetuated which must discourage men of quality from entering general practice.—ED. L.

INTESTINAL RUPTURE FOLLOWING NON-PENETRATING INJURY

SIR,—In your issue of April 16, Mr. Flavell illustrates dramatically, by his description of a rare complication of body-line bowling, an insidious disaster which may follow a blow upon the abdomen. The damage to the abdominal contents may be most extensive though the patient may show little signs for some hours of the extent of the injury. It is because of some recent experiences with such cases that we wish to reinforce the moral which he points "that the blow on the abdomen must be watched with no less attention than is the blow on the head."

In the last 10 cases admitted to the Radcliffe Infirmary with rupture of the small bowel resulting from a closed injury of the abdominal wall, some interesting features were noted. Of these 10, 7 survived the disaster; all these cases were operated on within twelve hours of the injury. Of the 7 survivors, 3 had partial tears of the small bowel which were sutured; 3 had complete transverse tears and were treated by anastomosis of the damaged ends; in the remaining case it was necessary to perform a local resection with anastomosis. Of the 3 patients who died, the first, who had been crushed by a falling wall, had a resection within twelve hours, but death resulted on the fifth day from anuria; in the second, a child of $2^1/_2$ years with associated head and leg injuries, the diagnosis was obscure for twenty-four hours, the patient dying of general peritonitis following operation; in the third, late suture, of the perforation was soon followed by death from general peritonitis. This case is detailed below (case 1).

In 6 of the 10 cases a definite latent period followed the injury, and this feature is illustrated by the other case described below (case 2).

CASE 1.—A gipsy boy, aged 17, was kicked in the abdomen by a horse just after midnight on Aug. 29, 1945. He was brought to the Radcliffe Infirmary about an hour after his injury, when he complained of abdominal pain but no shoulder-tip pain. Temperature and blood-pressure were normal; pulse-rate was 108 per min. The abdomen moved gently on respiration and showed slight generalised tenderness and resistance. Intestinal sounds were present. Rectal examination revealed no abnormality, and there was no blood in the urine. The injury did not appear severe, and there was some question at the time whether he should be admitted; but it was decided to keep him in hospital.

The following day, his condition was much the same, but that evening the pulse-rate rose and he vomited. Next morning the abdomen was rigid with generalised tenderness, and general peritonitis was obviously present. At laparotomy the abdominal cavity was found to contain purulent, foul-smelling fluid, and there were two perforations in the ileum. The proximal opening was oversewn and the lower opening was closed about an ileostomy tube. He was given penicillin and sulphonamide therapy, but his condition rapidly deteriorated and he died shortly before midnight the same day.

CASE 2.—A labourer of 33 was admitted to the Radcliffe Infirmary on Aug. 11 last year. Having drunk six pints of beer, he was bicycling home when he rode into a projecting iron bar which struck him in the abdomen. He felt winded and faint, but picked up his bicycle, pushed it home a quarter of a mile, put it away, and then lay on his bed. An hour and a half after the injury there was a gradual onset of dull pain all over the abdomen, and he noticed slight pain at the tip of both shoulders. He vomited about six times from midnight onwards until he was admitted to the Radcliffe Infirmary the next morning. Abdominal examination showed no evidence of external injury, but signs of generalised peritonitis.

Twelve hours after the injury, laparotomy was performed, the incision revealing that the right rectus muscle was partly torn across. The abdominal cavity contained free, brown, turbid fluid, and about 1 ft. from the duodenojejunal junction there was a complete transverse tear of the jejunum which extended into the mesentery. Also there were two small tears of the peritoneum over the transverse colon. After freshening the ends of the jejunum, end-to-end anastomosis was performed. The colon injuries were treated by a Lembert suture over the injured areas. The patient recovered, but convalescence was complicated by pelvic induration which resolved spontaneously.

The first case indicates that, though the patient may be in the hands of the surgeons within one hour of injury, the clinical picture may be sufficiently deceptive to cause fatal delay in operating. The second case emphasises that a severe abdominal rupture may be present yet the patient may "score ten runs" as in the case reported by Mr. Flavell, or may push a bicycle home as in this case. The moral, as Mr. Flavell has said, is that "on reasonable suspicion of perforation the belly should unhesitatingly be explored."

The Radcliffe Infirmary, Oxford. G. E. MOLONEY
J. N. WARD-MCQUAID.

HEALTH SERVICES BILL IN AUSTRALIA

SIR,—In your issue of Jan. 8, your Australian correspondent wrote of this Bill: "Dentists would also come under the scheme, and the government would pay half the fee." Here your correspondent was in error. At no time has the government intimated that it would pay any portion of the dental fees of the community. The known intentions of the government are summed up in the paragraphs following the statement under discussion in your correspondent's report.

GERSHON BENNETT
Melbourne. Hon. Secretary, Australian Dental Association.

WERTHEIM'S OPERATION

SIR,—Mr. John Stallworthy in your last issue advocates coöperation, as between radiotherapists and gynæcological surgeons, in the treatment of carcinoma of the cervix. To use a present-day vulgarism, "I couldn't agree more." But I do wish that he would give a place to "deep" X-ray therapy in his armamentarium, and to a physicist in his team. At Guy's Hospital a deep X-ray therapy department was established in 1923—26 years ago. From that time, we were in the habit of combining radiotherapy of this type with the Bonney-Wertheim operation. In my own cases I feel that any good and lasting results have been largely due to preoperative and postoperative radiation. Personally I find it difficult to believe that the combination of *radium* and the radical operation represents the ideal treatment, as they roughly cover the same field to the possible exclusion of the periphery.

London, W.1. FRANK COOK.

FEMALE CIRCUMCISION IN THE SUDAN

SIR,—I read with much interest the Parliamentary report on this subject which appeared in your issue of Feb. 26, and the letter by Sir Basil Neven-Spence published on March 12.

In view of what has appeared in your columns it may be of interest to record that during the years 1944–46, when I held in the Sudan Medical Service the appointment of assistant medical officer of health (special duties), I was engaged in a survey of public health and social medicine which included duty as school medical officer for all girls' schools in Khartoum province. This duty entailed the examination of all girls attending the primary and secondary schools and the Girls' Training College in Khartoum, Khartoum North, Omdurman, and rural schools in that province. I had therefore the opportunity of carrying out a complete medical examination.

Of a total of 3002 girls examined during the period of that survey, 1488 had been circumcised. Of these, 1103 had undergone the severe Pharaonic type of mutilation, and 385 the mild or sunna form. No difficulty was encountered in combining this special examination with that required in the general medical survey, and it was effected in a simple matter-of-fact manner which caused less trouble than a normal throat examination. The medical survey and general examination of the pupils attending the girls' schools had full coöperation from the

Digitized by Google

controller of girls' education of the Sudan education department.

An analysis of the various nationalities and religious communities of the girls examined and those subjected to circumcision showed that children of nationalities other than Sudanese and Egyptian and of religions other than Islam had undergone the practice.

The details of this particular survey should be recorded with the medical officer of health, Khartoum, and would be included in the school medical officer's report for those years.

Benghazi, Cyrenaica. ALICE I. MUIR LEACH.

CLINICAL ESTIMATION OF BASAL METABOLIC RATE

SIR,—Interesting as has been the article and correspondence on the relation between the R.P. index and the B.M.R., I am surprised that it has been published, because there is an excellent objective method of settling the problem, and of stating the relation in the form: "if the R.P. index is x, then the most probable value of the B.M.R. is y, and the odds are z to 1 that it is greater than +15% (or lower than −15%).

The method is, of course, statistical. Though one cannot expect the average practitioner to be an expert statistician, many are acquainted with the subject sufficiently to enable them to offer an opinion on whether a series of observations is suitable for statistical analysis; and, if the analysis is beyond their powers, to suggest to whom application might be made for assistance.

The problem under discussion is eminently suitable for statistical analysis, using the method of multiple regression, or perhaps by devising a suitable discriminant function. Discussion without such analysis reminds me of Kipling's chimera bombinating in a vacuum.

It would be, of course, much better to consult the statistician before accumulating the data.

Teddington, Middlesex. GEORGE DISCOMBE.

ERGOTHIONEINE IN URINE

SIR,—In her article of April 16, Dr. Work, says that ergothioneine is found in normal urine to the extent of 130–300 mg. per litre, and she followed its excretion in clinical trials of ergothioneine as an antithyroid active substance.

I have examined a number of normal urines by paper partition chromatography and have been unable to detect any ergothioneine in any of them, although a concentration of 5 mg. per litre could easily have been detected by my method. The main difference between Dr. Work's method and mine is that she relies on the colour reactions on spraying the sheet of filter-paper with Folin-Marenzi or Pauly reagents, while I have found both these too non-specific and have come to rely exclusively on the Hunter[1] colour reaction.

In this method the sheet of filter-paper is sprayed with a slightly modified Pauly reagent and then, after 30 sec., with 40% caustic-soda solution. The use of this very concentrated alkali was found essential. Ergothioneine develops an intense crimson colour over a period of 10 min., the only other substance that has been found to give a comparable colour being the breakdown product of ergothioneine (after a Hofmann degradation)—2-thiol-urocanic acid, which has a different R_F value.

The two main features are the specificity of the colour developed and its intensity. With weaker alkali (10% caustic soda or 30% potassium carbonate) ergothioneine gives a pale orange colour almost indistinguishable from that given by several substances normally present in urine, one at least having the same R_F value as ergothioneine in lutidine-collidine. No substance in urine gave the crimson spots corresponding to ergothioneine or 2-thiol-urocanic acid on spraying with 40% caustic soda, while ergothioneine, added to urine, gave a crimson spot in the expected position. The size of this spot corresponds closely to that from the same amount of erothioneine in water.

Dr. Work appears to rely chiefly on the high R_F value of ergothioneine in phenol. However the band of R_F 0·8 in phenol found by her in urine can be resolved into three bands by using p-cresol as solvent, all three bands reacting with the Folin-Marenzi reagent and one, the strongest, having an R_F value higher than that of ergothioneine.

With two substances of similar R_F value giving a non-specific reaction with, say, the Folin-Marenzi or Pauly reagents, it is clear that adding one (ergothioneine) will intensify the total colour due to both together without proving that the original colour was due to ergothioneine.

The identity of Dr. Work's and my ergothioneine was proved by an exchange of material.

It is worth mentioning that the filter-paper used was Whatman no. 531 which, unlike no. 1 and no. 4, resists concentrated alkali. This filter-paper is used routinely in the amino-acid chromatography which is the main work of this laboratory. No. 531 paper has the further advantages that it is appreciably faster than no. 4, is thinner, and is considerably tougher when wet.

Much more work on this problem of the estimation of ergothioneine has been done in collaboration with Dr. A. Lawson, and the results will be published elsewhere.

L. I. WOOLF
I.C.I. Research Fellow,
Institute of Child Health.

Hospital for Sick Children,
Great Ormond Street,
London, W.C.1.

1. Hunter, G. *Biochem. J.* 1928, **22**, 4.

SCORPION STINGS

SIR,—Your issue of April 2 (p. 591) mentioned the serum treatment of scorpion stings practised at the Pasteur Institute of Algeria. I should like, if I may, to call attention to a form of treatment which in my experience has always relieved the intense pain of these stings within 25 seconds.

During seven years of my service in India, I was stationed in localities where scorpions were commonly seen at certain periods of the year, and the cases I treated numbered over a hundred; the same method was successful in the case of my pet dogs stung by scorpions. Apart from a stimulant mixture given to overcome shock in some of the cases, the treatment consisted merely in applying to the site of the sting a swab soaked in rectified spirit containing scorpion venom obtained in the following manner:

The scorpion, alive and uninjured, is thrust into a wide-mouthed bottle containing sufficient spirit to obviate killing by drowning. In its fury and death-struggles, it lashes out against the sides of the bottle exuding at each stroke of its tail a tiny blob of white liquid discernible above the level of the spirit. A stock of 4 oz. of this spirit, containing as many as eight scorpions, retained its potency up to two years.

Before this treatment was adopted, injections of morphine or procaine were used; but unfortunately pain recurred four hours later. Rectified spirit alone, and rectified spirit to which dead scorpions were added, were both tried with definitely negative results. Whether artificially extracted venom added to spirit would serve as well, I do not know.

Bedford. J. O. DEWEY.

BENADRYL IN THE TREATMENT OF PARKINSONISM

SIR,—I should like to record the beneficial effects I have found with 'Benadryl' in the treatment of a case of parkinsonism.

A 60-year-old Greek woman with a 2-year history of classical parkinsonism, with no history of previous encephalitis, was given benadryl 50 mg. four times daily. She continued taking tinct. stramonii minims 15 thrice daily which she had been doing for the past 18 months.

After a week of this combined therapy she experienced great relief of symptoms generally and a marked improvement in her ability to get about. Rigidity and nocturnal muscular cramps were particularly alleviated. Tremor was improved in one hand but remained about the same in the other. She experienced some somnolence in the early stages of this combined therapy but this passed off after 10 days.

These findings correspond closely with those of Dr. Ryan and Dr. Wood (Feb. 12).

The stramonium was gradually decreased until a dose of minims 5 thrice daily was reached; the improvement remained unaffected.

British Military Hospital, Salonika. B. W. PERLOW.

Digitized by Google

CONGESTIVE HEART-FAILURE

SIR,—Since our article of April 9 was written, Dr. Reid has taken up a post overseas. I think, however, that I can reply to Mr. Cosin's query last week regarding the relation between hypoproteinæmia and œdema in obstinate cases.

We discussed this question at length, and at one stage we had the plasma-protein content determined as a routine. The problem is complicated. In the first place, in patients of the age-group we investigated, hypoproteinæmia is common whether or not they are in congestive failure. Secondly, mercurials commonly produce diuresis and loss of weight in nutritional œdema. Thirdly, in cases where the œdema clears up there is not necessarily a parallel rise in the plasma content. This is true for nutritional œdema as well as for "pure" congestive failure.

All the same, the possibility that in many cases malnutrition leads to congestive failure, through the mechanism of hypoproteinæmia, must be considered. In obstinate cases, some of the good results we attribute to prolonged rest and sodium restriction may be due to the nourishing diet. Incidentally a feature of congestive failure which often impressed Dr. Reid and myself was that these patients never, except in the very acute stage, suffer from lack of appetite.

Belmont Road Hospital, Liverpool. WILLIAM HUGHES.

PHYSICAL MANIFESTATIONS OF EMOTIONAL DISORDER

SIR,—May I enlarge a little on the last seven lines of my article of April 9? There are at least six conditions commonly associated with "worry," "anxiety," "strain," or the like. These are diabetes, fibrillation, duodenal ulcer (with digestive disturbance), high blood-pressure, insomnia, headache. I have the first two, but I have an absolutely first-rate digestion, normal blood-pressure, no insomnia, and no headache. Now, what sort of emotional condition is associated with what sort of physical symptom? If one has practically any physical manifestation and practically any emotional strain, practically any psychologist will instantly correlate the two, with a knowing smile. I still look forward to hearing of a psychologist who says, "Yes, but you've got just the physical symptoms I shouldn't expect in your circumstances," instead of just saying, "Well, there you are!"

DISABILITY NO. 27.

ŒSOPHAGEAL LESIONS IN SCLERODACTYLY

SIR,—The association of œsophageal lesions with sclerodactyly reported by Dr. Bourne in his article of March 5 is interesting from many points of view. The tracings of radiographs which he shows could all be explained as varying stages of peptic ulcer of the œsophagus or œsophagitis with sliding hernia of the stomach into the mediastinum. Such pictures have been described in conjunction with Dr. A. S. Johnstone.[1]

The first tracing corresponds to that of sliding hernia, patulous cardia, and œsophagitis; the second to that of complete obstruction due to submucous fibrosis; the third to a long fibrous stenosis; and the fourth to a short fibrous stenosis. All of these types are described in our paper and were confirmed by œsophagoscopy, biopsy, and operation. Incidentally the second tracing is not like that seen ever in achalasia or cardiospasm.

Our suggestion that all these patients described by Dr. Bourne are suffering from peptic ulceration of the œsophagus and not sclerodermia of the œsophagus is supported by the frequent association reported in other papers quoted by Dr. Bourne and the failure to obtain histological evidence of anything other than œsophagitis or simple ulceration. This raises the question of a possible ætiological association between sclerodermia and some cases of sliding hernia with peptic ulceration of the œsophagus. We are not in a position to give a decisive answer to this, but it may widen the horizon a little by reporting that in well over a hundred patients with peptic œsophagitis or ulceration studied in the thoracic surgical department at Leeds there has been no example of sclerodermia, and of 60 patients with cardiospasm none had changes in skin or muscles.

Our experience is that peptic œsophagitis is a fairly common condition in hospital practice. The reasons it is not diagnosed more often are, firstly, that the radiology of the condition is difficult and that it may be missed by the expert unless he is asked to look for it by the clinician, and secondly that those with obstructive lesions tend to be treated by dilatation or by gastrostomy without the diagnosis being made. It is therefore unwise at this stage to draw any deductions from the described association with sclerodermia, and it is not justifiable to assume that the lesion in the œsophagus has the same pathology as that in the skin and muscles. The possible relation between sliding diaphragmatic hernias and sclerodermia needs further detailed investigation with more accurate records both from the dermatological and œsophageal points of view.

Leeds. P. R. ALLISON.

1. Allison, P. R. *Thorax*, 1948, 3, 20.

LOUPING-ILL

SIR,—From their most interesting account last week of this disorder, Dr. Brewis and his colleagues seem to have had some difficulty in removing the ticks.

This is not difficult. 'Vaseline' rubbed in will kill the ticks by obstructing their breathing spiracles, which are not buried. The buried head is anchored in the skin by small hooks. These gradually relax after death, and in an hour or so the beasts are easily removed by scraping with the back of a knife.

West Malvern. F. H. JACOB.

STREPTOMYCIN IN HUMAN PLAGUE

SIR,—I should like to reply to the observations of Prof. Bradford Hill and Dr. Bhagwat on the article of Jan. 15 by Dr. Rao and myself. Prof. Bradford Hill (Jan. 29) says:

1. That "pseudo-statistical 'evidence' like this must damage rather than further" the case for streptomycin in human plague.—Here time has already given the verdict; my observations have been confirmed.[1] Streptomycin needs no statistical prop. What statistical prop was produced to prove the efficacy of penicillin in gonorrhœa or N.A.B. in syphilis? Certain drugs give such striking results that their value becomes apparent straight away. Streptomycin in plague is such a one.

2. That the figures do not support the claim that immunity develops a week or so after inoculation, and no basic data are given to the reader.—The basic data are not in my possession at present, as I was transferred from the place of original work sixteen months back. I am calling for these data and will deal with this point later.

3. That out of 15 moribund cases, 12 recovered, and that, well-documented, this would be impressive evidence.—You will recall, Sir, that I submitted temperature charts, &c., which were omitted from considerations of space. I wish you had mentioned this yourself in reply to observations of Prof. Bradford Hill as coming from the editor.

4. That it was misleading to refer to the brilliant success of streptomycin therapy, under which no patient died who was not already moribund.—All that I meant to convey was that the patients who died were already moribund when treatment started, and there is nothing in our previous statements which is inconsistent with this.

To the comments of Dr. Bhagwat, I reply as follows:

1. The inoculations were given in several villages, some miles apart. Only a skeleton staff was at my disposal.

2. I have already said that inoculation perhaps gave a slightly better chance of survival.

3. All cases treated with streptomycin were uninoculated.

I am grateful to Dr. Bhagwat for drawing attention to new aspects, which I shall bear in mind.

P. V. KARAMCHANDANI
District Surgeon, Bellary, India.

1. Sokhey, S. S., Wagle, P. M. *Proc. 4th Internat. Conf. trop. Med. Malaria.* Washington, 1948. Wagle, P. M., Bedarkar, M. K. *Ind. med. Gaz.* 1948, 83, 406.

Digitized by Google

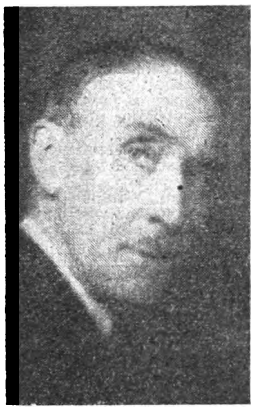
Obituary

JOHN RONALD CURRIE

M.A. OXFD & EDIN., M.D., LL.D. GLASG., F.R.C.P.E.

Dr. J. R. Currie, emeritus professor of public health in the University of Glasgow, died at his home in Edinburgh on April 13.

His academic career was remarkable. From Ayr Academy and the University of Edinburgh, where he took his M.A. in 1891, he proceeded to Lincoln College, Oxford, with an open scholarship, and gained a first in classical honours moderations, graduating B.A. in 1896. In due course he entered the medical school of Glasgow, and in 1898 he graduated M.B. with commendation. In 1910 he was awarded the degree of M.D. with high commendation, for his thesis on serum-sickness in man. This work was, incidentally, some of the earliest done on the subject. He was elected F.R.C.P.E. in 1934, and on his retirement from the chair of public health at Glasgow in 1940 the university conferred upon him its honorary degree of doctor of laws.



[Davidson

Currie's early experience of preventive medicine was gained in the sanitary department of Glasgow, under the late A. K. Chalmers, and later in the counties of Stirling and Dunbarton, where he acted for a time as medical officer. With these duties he combined that of an assistant investigator with the Royal Commission on the Poor Law and at this early stage showed in his reports the lucidity and style which to the last characterised his writings. His first charge came in 1909 when he was appointed medical officer of health for the city of Chester, and in 1910 he took up a similar appointment for Fife and Kindross. A year later he joined the staff of the Scottish Insurance Commission. His administrative career was interrupted by his service with the R.A.M.C. during the first world war in France and Italy and later as a specialist officer to the Scottish and Southern Commands. In his *Mustering of Medical Service in Scotland during the War* (1922) he gave a vivid account of the building up of the Army medical administration.

Shortly after demobilisation Currie joined the Scottish Board of Health, where he remained until 1922, when he was appointed professor of preventive medicine at Queen's University, Kingston, Ontario. The following year the Henry Mechan chair of public health was founded at Glasgow and he was its first occupant. The appointment offered him the ideal opportunity to exercise his outstanding talent for administration. He developed new laboratories and created a coördinated syllabus for the diploma in public health which became a model. His organising and administrative abilities were early recognised by the university, and he was in turn elected dean of the faculty of medicine and clerk of senate. Throughout his tenure of the Glasgow chair he combined with his teaching duties those of medical officer of the estuarine county of Bute, an appointment which enabled him to bring a strong practical flavour to his lecture courses.

A. G. M., to whom we owe this memoir, adds: "Currie was not an easy man to know, but those who were close to him soon perceived the simplicity and high integrity of his character. He was a master of classical allusion, and had a dry and often mordant wit. He would not tolerate slipshod work either by himself or by those whom he chose to work with him. His students looked upon him with affection as one of the Old Guard of professors who were scholars and gentlemen. His hobbies were literary and erudite, as witness his habit of borrowing from the library the same Dumas novel in French, German, and Italian and working out the errors which had crept in during the cross-translations.

"Essentially practical in his outlook, he had some trenchant things to say of the more superficial exponents of social medicine. 'Administration can be learnt in the field, but science must be taught,' he used to remark, and on this view were based his textbooks, which are today standard works. But he was not a diehard, and he would follow wherever a new trail led if the goal were likely to be worth while."

Prof. Currie married in 1901 Miss Sara Browne, of Parton, Kirkcudbrightshire, who survives him with one daughter.

HOWARD BLUNTISHAM HODSON

M.D. LOND., M.R.C.P., D.P.H.

Dr. Howard Hodson, clinical tuberculosis officer to the Norfolk county council, died at his home in Colchester on April 18.

Born at Chingford, Essex, in 1906, he was educated at Merchant Taylors' School and St. Thomas's Hospital. After qualifying in 1929 he held house-appointments at St. Thomas's and at Brompton Hospital Sanatorium, Frimley, till in 1932 he was appointed assistant medical officer at Grove Park Hospital. The following year, while holding a resident post at Bolingbroke Hospital, he took his M.D. In 1935 he returned to Grove Park Hospital as senior assistant medical officer, and later he held the same post at the High Wood Hospital for Children. In 1938 he was appointed tuberculosis officer for the western area of Norfolk.

At the beginning of the war in 1939 Hodson joined the R.A.M.C., and in 1942 he had reached the rank of lieut.-colonel, serving on the staff of the hygiene directorate at the War Office; later he became assistant director of hygiene at the War Office, a post always previously held by a regular R.A.M.C. officer.

A colleague writes: "Howard Hodson was a bachelor, and a most amiable and likeable character, loyal to a degree, with a great sense of duty, tempered as it should be with good humour and tact. His pleasing personality was well received by his colleagues, and his patients appreciated his skill and kindness."

CHARLES WILLIAM MENELAUS HOPE

O.B.E., M.D. DURH., F.R.C.S.

Mr. Charles Hope, consulting surgeon for diseases of the ear, nose, and throat to King's College Hospital, London, died at Knaresborough on April 21 at the age of 68.

Educated at Clifton College and the University of Durham, where he graduated in 1903, he came to London soon after qualifying. At first he was attached to St. Mary's Hospital as a clinical assistant in the throat department under Dr. William Hill, but in 1914 he was appointed to the staff of King's College Hospital as assistant surgeon for diseases of the nose and throat under Sir StClair Thomson. When in 1932 the aural and the nose and throat departments were joined, he became head of the new combined department and remained in charge until his retirement in 1941. He was also consulting surgeon for his specialty to the Finchley Memorial Hospital and the Royal Eye Hospital, Southwark.

During the 1914–18 war he was attached as a surgeon to the St. John Ambulance Brigade Hospital, B.E.F., with the rank of honorary major R.A.M.C. For his services he received the O.B.E. and was made an officer of the Order of St. John of Jerusalem. At the beginning of the late war he joined the Emergency Medical Service as a full-time surgeon, and he was posted to Horton Emergency Hospital, Epsom, where he worked until his retirement, owing to ill health, in 1941.

Mr. Hope took a great interest in all the activities of King's College Hospital medical school and its students. For many years he was president of the students' club and societies' union, where his wise counsel and shrewd judgment were much appreciated, and to more than a generation of students and residents he was known affectionately as Charlie Hope.

T. C. writes: "Hope was an outstanding surgeon with a wonderfully gentle pair of hands. Those who were fortunate enough to work with him learnt and remem-

Digitized by Google

bered much more from the example set by his thoroughness, patience, kindliness, and dexterous touch than they would from any formal teaching, and his compelling personality attracted the interest and attention of all with whom he came into contact. A keen fisherman and gardener, and no mean carpenter, he was interested in knowing how anything worked; but in all things, whether in work or in play, he insisted on the best. His instruments and equipment were always in full working order and in the right place at the right time; his roses and dahlias the biggest and best; the coffee that he ground himself for his guests, the most fragrant; and his annual pilgrimage to Scotland after the salmon, most carefully prepared for and usually fruitful, as so many recipients of a fine, fresh salmon appreciated. He was a bachelor whose kindliness and generosity ensured him a wide circle of friends, and he will never be forgotten by those who worked with and learnt so much from him."

JOHN WARDLE BONE

M.B., B.SC., LL.D. EDIN.

Dr. J. W. Bone, who died at Luton on April 14 at the age of 79, had given distinguished service to his profession and to his town. At the time of his death he was senior treasurer of the General Medical Council and he had but lately retired from the same office in the British Medical Association. Speaking at his memorial service the Vicar of Luton truly said that there was no need to build a monument to him, for his greatest monument was the hospitals of the town.

The eldest son of the late Jacob Rowell Bone, of Newcastle-on-Tyne, he was educated at the School of Science there and the University of Edinburgh, where he graduated M.B. with first-class honours in 1891. Shortly afterwards he settled in practice in Luton where all his working life was spent.

Dr. Bone's connexion with the Children's Hospital went back to the time when it was known as the Luton Children's Sick and Convalescent Hospital. He worked there from 1895, joining the staff four years later, and in 1905 he became honorary medical superintendent, an appointment he held until his retirement in 1933. He saw the expansion of the hospital from 14–15 beds to 40–50 beds, and his practical suggestions proved of much value in its development. His associations with the Bute Hospital and the Luton and Dunstable Hospital were of equally long standing, and even after his retirement he continued to be an active member of the hospital management committee. One of the prime movers for the improvements carried out at the hospital in 1933, he also worked enthusiastically in the building of the new Luton and Dunstable Hospital which replaced the Bute Hospital, and it was a fitting recognition of his interest in the hospital when in 1938 he was elected president.

"In Luton," says a fellow townsman, "Dr. Bone was held in respect for his firm personality and his fighting qualities. From my own contact with him, I know that he was a hard hitter, but I am sure he expected hard hitting from those who held different views to his own, and was much too big a man to resent them. I think it is true to say that he was a man who did not suffer fools gladly, but the smile which accompanied his sometimes caustic comments gave the lie to any suggestion of vindictiveness."

Dr. Bone joined the British Medical Association in 1905 and became prominent in its counsels. It was natural that he should be appointed to the general-practice committee; but his membership of the central ethical committee, and of committees on certification for workmen's compensation, on health services, on lunacy law and mental disorders, on medical education, and on poor-law reform, and his chairmanship of the medico-political committee, showed the scope of his interests. Last year, when he retired from the treasurership, which he had held for nine years, he was awarded the gold medal of the association, given "only once in a decade" for conspicuous services.

In 1928 Dr. Bone was returned to the General Medical Council as a direct representative of the profession; in the following year he was elected to the pharmacopœia and public-health committees and in 1939 he became one of the council's treasurers. He took great interest in the work of the council, especially in the consideration of penal cases, and he has been one of its most active and zealous members. As treasurer and chairman of the finance committee he took the chief part in working out plans for the restoration of the council's buildings after war damage. He was always considerate to the office staff, and for his kindliness he will be much missed by them as well as by his fellow members of the council.

Dr. Bone had also served on departmental committees of the Ministry of Health on morphine and heroin addiction and on the training of midwives. In 1946 he was awarded the honorary degree of LL.D. by the University of Edinburgh. His wife died some years ago and he leaves two sons and a daughter.

Appointments

ANDERSON, W. L., M.B. Glasg.: asst. chest physician, Manchester.
COELLO, A. J., L.M.S. Barcelona, D.P.H.: asst. chest physician, Barrow in Furness.
DAVIES, H. J., M.B. Lond., D.P.H.: H.M. inspector of factories.
*KEITH, GLADYS, M.B.LOND., F.R.C.S., M.R.C.O.G. visiting obstetrician and gynæcologist, Tottenham Health Centre.
PARKER, W. S., M.B. Manc., D.P.H., D.I.H.: M.O.H., Brighton.
SHAFAR, JACOB, M.D. Glasg., M.R.C.P., D.P.H.: asst. chest physician, central and east Lancashire.
SLATER, H. B., M.B. Manc.: asst. chest physician, Manchester.
WATERS, H. S., M.A., M.B. Camb., F.R.C.S., F.R.C.O.G.: obstetrician and gynæcologist, Blackburn and District Hospital Centre.

* Amended notice.

Births, Marriages, and Deaths

BIRTHS

ARMIN.—On April 18, the wife of Dr. R. H. Armin—a daughter.
BEVAN.—On April 12, at Hertford, the wife of Dr. Carus Bevan—a daughter.
CAREY.—On April 16, at Lewisham, the wife of Dr. C. F. Carey—a daughter.
CLARKE.—On April 13, at Bognor, the wife of Mr. E. P. Clarke, F.R.C.S.—a son.
EWELL.—On April 14, at Cowes, the wife of Dr. E. J. Ewell—a daughter.
HARRISON.—On April 17, at Farnborough, Kent, the wife of Dr. R. J. Harrison—a son.
MCGAVIN.—On April 22, at Leicester, the wife of Mr. Donald McGavin, F.R.C.S.—a son.
MAYNE.—On April 19, the wife of Dr. A. H. Mayne—a son.
MILLER.—On April 16, in Edinburgh, the wife of Dr. R. A. Miller—a daughter.
NORMAN.—On April 21, the wife of Dr. Oliver Norman—a son.
REID.—On April 13, at Oxton, the wife of Colonel James Reid, late R.A.M.C.—a son.
ROEMMELE.—On March 27, at Stornoway, the wife of Mr. P. M. Roemmele, F.R.C.S.—a son.
SIMS.—On April 21, at Windsor, the wife of Dr. T. H. Sims—a son.
SWEET.—On April 17, the wife of Dr. R. D. Sweet—a daughter.
WHITTINGHAM.—On April 14, at Fleet, Hants, the wife of Flying-Officer D. G. V. Whittingham, M.B.—a son.
YEATES.—On April 3, at Newcastle-on-Tyne, the wife of Mr. W. K. Yeates, F.R.C.S.—a daughter.

MARRIAGES

FRAIN-BELL—SHARP.—On April 15, at St. Andrews, William Frain-Bell, M.B., to Catherine Elaine Easson Sharp, M.B.
HAYTER—HALLETT.—On April 21, at Woodham, Woking, Anthony Goodenough Hayter, B.M., to Elizabeth Marion Hallett.
LEWIS—CALDWELL.—On April 9, in Edinburgh, Ian Calder Lewis, M.B., to Cynthia Caldwell.
THOMSON—MOWAT.—On April 14, at Halifax, George William Rosslyn Thomson, M.B. to Mary Stewart Mowat, M.B.

DEATHS

BARKER.—On April 20, Chesman Barker, M.B. Lond., aged 80.
BONE.—On April 14, John Wardle Bone, M.B., B.SC. Edin, aged 79.
CHURCHILL.—On April 23, Joseph Henry Churchill, M.R.C.S.
CURRIE.—On April 13, in Edinburgh, John Ronald Currie, M.A. Oxfd, M.D., LL.D. Glasg., D.P.H., F.R.C.P.E.
ECCLES.—On April 24, at Driffield, Yorks, Robert Burton Eccles, M.R.C.S.
HALLIDAY.—On April 18, at Lacey Green, near Princes Risborough, Bucks, John Rutherford Halliday, M.D. Durh.
HOCKEN.—On April 16, at St. Austell, Cornwall, Melville Hocken, M.B. Lond.
HOPE.—On April 21, at Knaresborough, Charles William Menelaus Hope, O.B.E., M.D. Durh., F.R.C.S.
MACKAY.—On April 12, at Campbeltown, Argyll, Duncan Matheson Mackay, M.D. Edin., aged 79.
MACKELLAR.—On April 21, at Dewsbury, John Donald Matheson MacKellar, M.B. Glasg.
MCKETTRICK.—On April 14, Frederick John McKettrick, M.B. Edin., aged 84.
MELVILLE.—On April 14, in London, Charles William Francis Melville, C.B., M.B. Edin., F.R.C.S.E., major-general, I.M.S. retd.
NEILSON.—On April 13, at Woking, Surrey, Henry John Neilson, C.B.E., M.D. Glasg., aged 86.
PAWSON.—On April 12, at Dyserth, Flintshire, Edward Basil Pawson, M.B. Camb.
POLLOCK.—On April 22, Edward Stoute Pollock, B.A., M.D. Dubl.
RICHARDS.—On April 18, at Monkleigh, Bideford, Owen William Richards, C.M.G., D.S.O., M.A., D.M. Oxfd, F.R.C.S.
WARNER.—On April 20, at Exeter, Harold Percy Warner, M.B. Lond., aged 63.

Digitized by Google

Notes and News

THE NATIONAL FORMULARY

ON May 1 the new *National Formulary* comes into operation; and the Ministry of Health urges that the use of earlier formularies should be discontinued. The use of *N.(W.)F.* or old *N.F.* titles will cause inconvenience and delay to the pharmacist, who may have to refer the prescription back to the doctor. All formulæ that are not contained in the *B.P.*, *B.P.C.*, or *N.F.* should be written out in full. The new formulary, composed by an expert committee of the medical and pharmaceutical professions, is more comprehensive than earlier editions.

STRENGTHENING THE RED CROSS

EVERY new war shows new ways in which the Red Cross can help its victims if only it is allowed. A diplomatic conference is now being held at Geneva to consider the amendments and additions adopted last year at Stockholm by 50 governments and 52 red-cross societies to the international conventions which govern the work of the organisation (*Times*, April 21, p. 5). The first of the conventions under revision is the Geneva convention of 1929 which governs the relief of wounded and sick combatants. Here there is a return to the principles of Henry Durant, the Swiss observer of Solferino, who started the Red Cross. Local populations are to be encouraged to give first-aid to the wounded and are not to be penalised for doing so even if the wounded are enemy parachutists. Under this convention are also proposed rules for the protection of army medical personnel. As under the existing convention, they are not to be considered as prisoners, though they are to enjoy the same rights; they are to be repatriated as quickly as possible—except any who may be needed to look after the wounded, and these are to be on the same footing as the medical personnel of the captors. It is also hoped that the medical personnel of all armies will wear the same distinguishing badge. The amendments to the Hague convention extend these provisions to maritime warfare. The third international convention deals with the treatment of prisoners-of-war. It is now proposed to prohibit collective punishment by curtailing prisoners' food. The daily rations must now be sufficient to keep the prisoner in good health, for experience in the Far East proved that the former provision, that it must be equivalent to that of the reserve forces of the detaining Power, can be inadequate. No prisoner may be physically mutilated or subjected to scientific experiment. A fourth convention for the protection of civilians was only in draft in 1939. The late war showed only too clearly the dangers and disabilities to which civilians are now exposed, and the new convention seeks to extend its protection to them whether they are involved in a civil or international conflict.

GERMAN EXPERIMENTS IN WATER PURIFICATION

THE modern soldier's lot has been described as "waiting for something to happen on a diet of M. & V. and chlorinated water." The unpleasantness of chlorinated water was offset in the late war by the absence of any large outbreaks of water-borne disease; and usually the addition of "de-tasting" tablets provided a fluid that was bland, if unexciting. The Germans used their ingenuity to modify existing methods, and to devise new methods, of purification.[1] It was found, for instance, that the life of Berkefeld filters could be prolonged by the incorporation in the kieselguhr of finely divided silver, which delays formation of the bacterial clot that in the end makes such filters unserviceable. Silver was also tested in the purification of small volumes of water under field conditions. Previously the disadvantages of metallic methods were the waiting-time necessary before purification was complete, and the adverse effect of suspended matter in the water. But German research showed that by incorporating silver chloride in sodium chloride and activating the mixture with an oxidising agent, immediate sterilisation could be produced; and an ingenious pack including two paper filters allowed the process to be carried on as the water was poured into the service water-bottle. So successful did this method prove that such outfits are now on sale to the civilian population of eastern Germany, and they are in great demand. No doubt in the laboratory this method is foolproof; but sand-storms and monsoons would give short shrift to paper filters and chemicals which must be kept dry up to the moment of use.

Another example of ingenuity may be found in the methods of testing the purity of water in the field by passage through a nitrocellulose filter of a porosity that will hold back bacteria. The resulting filter-film may be either examined directly or impregnated with nutrient culture media and incubated. It would be wrong to suppose that in surroundings where the mobile hygiene laboratories of our Army cannot penetrate, this method would give accurate results.

1. Fiat, final report no. 1312. Particulars from Board of Trade technical information and documents unit, 38, Cadogan Square, London, S.W.1.

INTERNATIONAL OCCASION AT QUEEN SQUARE

THE radiological department at the National Hospital, Queen Square, London, has for some time needed more space in which to deal with the growing number of ventriculograms, encephalograms, arteriograms, and myelograms. Dr. Erik Lysholm, of Stockholm, happened to be in London when the hospital authorities announced their proposal that the department should be moved to the third floor of the old building. This floor contained many small rooms, and the hope of successful adaptation did not seem bright; but in collaboration with Dr. Erik Lindgren and Mr. Molander, the Swedish government hospital architect, Dr. Lysholm, worked out a satisfactory solution. He died shortly afterwards, and the new department, opened by Dr. Lindgren on April 5, has been named after him. Four skull tables were supplied by Mr. G. Shönander, who presented one without charge to the hospital in memory of Dr. Lysholm; generating plant and tilting tables were provided by Philips Electrical Ltd. Through the Lysholm radiological department one more is added to the National Hospital's many international links.

A DIGEST OF HEALTH LEGISLATION

The International Digest of Health Legislation, of which the first issue has appeared[1] is the successor to the first section of the *Bulletin Mensuel de l'Office International d'Hygiène Publique*. Published by W.H.O., the *Digest* is intended for those interested in the administrative and legislative aspects of public health; and it will consist of reprints and translations of, or extracts from, the texts of the most important laws and regulations dealing with public health and related subjects adopted in different countries. It is published in separate editions in the English and French languages, and each edition is issued in two forms—as a bound periodical, and as a collection of separate fascicles in a loose cover for filing by subject or country.

WORLD MEDICAL ASSOCIATION BULLETIN

THIS *Bulletin*, of which the first issue has been published,[2] will print from time to time the results of surveys conducted by the association. Subjects at present under survey include the supply of doctors in all the great nations, medical education, the laws regulating medical practice, the manufacture of drugs and medical products and the laws regulating manufacture and distribution, and problems related to social security. The *Bulletin* announces that the association is to hold a general assembly in London from Oct. 6 to 15; Dr. Charles Hill is the president-elect.

ATOMIC BOMBS

THE trials of the two atomic bombs at Bikini atoll have been described by one of the numerous official participants.[3] His job was the detection of residual emanations in the air, water, target ships, and fish. Apart from a little moralising and some praise of tropical sunrises, the book is factual and interesting. Probably no planned experiment ever received more care and forethought, or employed a larger team of experts, but the author, like all of us, has little idea of what was learnt. It is rather as if we had a picture of Newton's garden, knew the species of apple which fell (no doubt a Newton Wonder), and had a verbatim account of Lady N's comments on the state of his clothes—without any mention of the word "gravity." However, Dr. Bradley makes up for this by giving a clear and succinct A.B.C. of atomic energy. His book is said to have caused much alarm among the reading public of the U.S.A.

1. Obtainable from W.H.O., sales section, Palais des Nations, Geneva; or from H.M. Stationery Office, P.O. Box 569, London, S.E.1. 6s. 3d.
2. Editor-in-chief, Dr. Morris Fishbein. Issued from 535, North Dearborn, Chicago 10, Ill.
3. No Place to Hide. By DAVID BRADLEY. London: Hodder & Stoughton. 1949. Pp. 191. 7s. 6d.

Digitized by Google

University of Oxford

Dr. Thomas Stapleton has been elected to a Radcliffe travelling fellowship.

University of Cambridge

A Pinsent-Darwin studentship has been awarded to Dr. John McFie.

University of London

On Tuesday, May 10, at 5.30 P.M., at the London School of Hygiene, Keppel Street, W.C.1, Prof. Jacques Tréfouël will describe Advances in Chemotherapeutic Research at the Pasteur Institute of Paris.

University of Sheffield

At a recent examination the following were successful:

Final M.B., Ch.B. (Parts II and III).—R. G. Ball, A. A. Belton, J. D. Bird, J. P. Caley, Philip Cauthery, Barbara J. Green, Mary A. Le C. Hills, J. D. Howard, Nansi M. Hutchinson, J. C. Johnson, L. C. W. Kershaw, R. G. F. Lampart, R. P. Lee, Margaret B. Lees, S. C. L. Ramesar, K. E. Spittlehouse, Betty M. Wylie.

University of Birmingham

On May 12, 13, 16, and 17 Prof. E. B. Verney, F.R.S., will deliver the William Withering lectures. He is to speak on the Excretion of Water by the Kidney with special reference to its Neurohypophysial Control. On May 19 and 26 Mr. Charles Read will give the Ingleby lectures, on Stress Incontinence of Urine in the Female. All the lectures will be held in the anatomy theatre of the medical school at 4 P.M.

University of Bristol

The council have decided to establish a chair of pharmacology next session, and they have appointed Dr. J. H. S. Heller to be the first professor. Dr. Heller at present holds the appointment of reader in charge of the department of pharmacology in the university.

University of Edinburgh

On Thursday, May 19, at 5 P.M., at University New Buildings, Teviot Place, Edinburgh, Prof. H. S. Raper, F.R.S., will deliver the Sharpey-Schafer lecture, on Fat Absorption and some of its Problems.

South-East Metropolitan Regional Tuberculosis Society

A clinical meeting of this society will be held on Saturday, May 14, at the Royal Sea-Bathing Hospital, Margate.

Closed Area

The Medical Practices Committee have decided that the number of doctors providing general medical services is adequate in the Minchinhampton district of Gloucestershire, and this district has accordingly been added to the list of closed areas.

Royal Institute of Public Health and Hygiene

On July 21, at 3 P.M. the Harben medal for services to public health will be presented to Lord Boyd-Orr, F.R.S., and the Smith award for noteworthy work in the discharge of official duties to Dr. M. T. Morgan, medical officer of health for the Port of London.

On Sept. 15, at 3 P.M., Dr. René Sand, professor of social medicine in the University of Brussels, will deliver the Bengue lecture on World Trends in the Teaching of Social Medicine and Public Health. Both meetings will be held at the institute, 28, Portland Place, London, W.1.

World Health Organisation

Dr. Martha Eliot, associate chief of the U.S. Children's Bureau, has been appointed an assistant director-general of W.H.O.

Dr. Eliot is a lecturer in pædiatrics at Yale University, and last year she received the Lasker award for distinguished service in public health. She has collaborated in large-scale child programmes in the U.S.A. and abroad, including the Emergency Maternal and Infant Care plan for families of U.S. servicemen, and she recently completed a survey of child health and welfare in the U.S. Zone of Germany. As delegate to international conferences, Dr. Eliot has taken part in the work of UNRRA and UNICEF, and she was chairman of the W.H.O. expert committee on maternal and child health.

Dr. Neville Goodman, a senior medical officer of the Ministry of Health, who has been acting assistant director-general, is returning to his post in England after the World Health Assembly terminates next July.

Royal Medical Benevolent Fund

The annual general meeting of this society will be held at 11, Chandos Street, London, W.1, on Friday, May 13, at 5.15 P.M., when Lord Webb-Johnson, the president, will be in the chair.

Institute of Hospital Administrators

The annual conference of the institute will be held at Southport on May 6 and 7. Further particulars may be had from the secretary, Tavistock House North, Tavistock Square, London, W.C.1.

Prof. J. C. Spence, Nuffield professor of child health at Newcastle-on-Tyne, will deliver the Cutter lecture in preventive medicine at Harvard University on May 11. He will serve also as visiting physician-in-chief for a week to the Boston Children's Hospital, and then travel to Canada to deliver the Blackader lecture at the annual meeting of the Canadian Medical Association in Saskatoon.

The editorship of the *British Journal of Urology* has passed to Mr. David Band, F.R.C.S.E., who may be addressed at the University New Buildings, Edinburgh.

Blood Group News is a new publication which lists contributions to the literature on this subject. The editor is Dr. P. H. Andresen, University Institute of Legal Medicine, Frederik Vs Vej 9, Copenhagen Ø, Denmark.

The journal *Marriage Hygiene* has now been reorganised under the title of the *International Journal of Sexology*, and regional editors for the main geographical areas of the world have been appointed. The members of the editorial board for the British Isles are Dr. Clifford Allen, Mr. Ambrose Appelbe, LL.B., Prof. F. A. E. Crew, M.D., F.R.S., Dr. E. Elkan, Mr. Kenneth Walker, F.R.C.S., and Dr. Helena Wright, with Mr. Cyril Bibby, M.SC., as editor.

A new Italian journal, *Annali Italiani di Pediatria*, began publication in December at Cagliari, the southern capital of Sardinia. The first issue (nos. 1–6) contains nine original articles, of which seven come from the University of Cagliari, one from the University of Sassari (the northern capital), and one from the University of Messina, Sicily.

Diary of the Week

MAY 1 TO 7

Tuesday, 3rd

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. N. Hamilton Fairley, F.R.S.: Malaria, with special reference to certain Experimental, Clinical, and Chemotherapeutical investigations. (First Croonian lecture.)

UNIVERSITY OF LONDON
5 P.M. (London School of Economics, Houghton Street, W.C.2.) Sir James Ross: National Health Service. (First of three lectures.)

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. F. R. Bettley: Psoriasiform Eruptions.

EDINBURGH POST-GRADUATE BOARD FOR MEDICINE
5 P.M. (University New Buildings.) Prof. H. W. Fullerton: Anticoagulant Therapy.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. (Wright-Fleming Institute). Prof. E. W. Rideal, F.R.S. Surface Properties of Bacteria (First of six weekly Almroth Wright Lectures on the Bacterial Cell).

Wednesday, 4th

UNIVERSITY OF GLASGOW
8 P.M. (Department of Ophthalmology.) Prof. W. J. B. Riddell: European Vacation.

Thursday, 5th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Hamilton Fairley: Malaria. (Last Croonian lecture.)

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. R. T. Brain: Physio- and Electro-therapy.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.15 P.M. Dr. I. Simson Hall: Surgical Treatment of Otosclerosis.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, S.W.1
4.30 P.M. Dr. Denis Williams: Neurology lecture-demonstration.

ROYAL PHOTOGRAPHIC SOCIETY, 16, Prince's Gate, S.W.7
7 P.M. (*Medical group.*) Dr. R. G. W. Ollerenshaw: Future of Medical Photography.

HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. A. Brownlie Smith: Developments in the Surgery of the Labyrinth.

Saturday, 7th

BIOCHEMICAL SOCIETY
1 P.M. (University Museum, Oxford.) Short papers and demonstrations.

Digitized by Google

Digitized by Google

Digitized by Google

Digitized by Google

Digitized by Google

Mar16'55
Oct12'55
Dec3'55
May19'64
Mar3'66
Jul16'68
Feb19'69

47185

Lancet

Mar.-Apr., 1949 v.1

Lancet
Mar.-Apr., 1949 v.1
47185

Iowa State Medical Library
HISTORICAL BUILDING
DES MOINES, IOWA

We hope you obtain pleasure and profit from the use of the Iowa State Medical Library. You can increase its usefulness by returning your books promptly. We are pleased to be of service to you.

Borrower. Adults are entitled to draw books by filling out an application card.

Number of Volumes. Two new books, or two new consecutive Journals cannot be taken by one person. Students may borrow 3 volumes at a time, which are not renewable.

Time Kept. The period of loan is two weeks; older books may be once renewed. New books and Journals are not renewable.

Forfeiture of Privilege. Loss of books or journals without paying for same, defacing or mutilating materials, three requests for postage without results, three requests for return of material without results, or necessity of asking Attorney General's aid to have material returned, bars from future loans.

Transients and those at hotels may borrow books by depositing the cost of the book, or $5.00, which is returned when the book is returned.

Digitized by Google